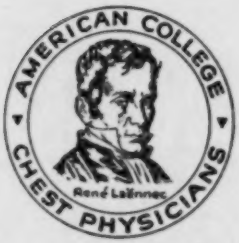
VOLUME XXI NUMBER 6

DISEASES

of the

CHEST

OFFICIAL PUBLICATION



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XII Congress, International Union Against Tuberculosis
II International Congress on Diseases of the Chest
Rio de Janeiro, Brazil, August 24-30, 1952

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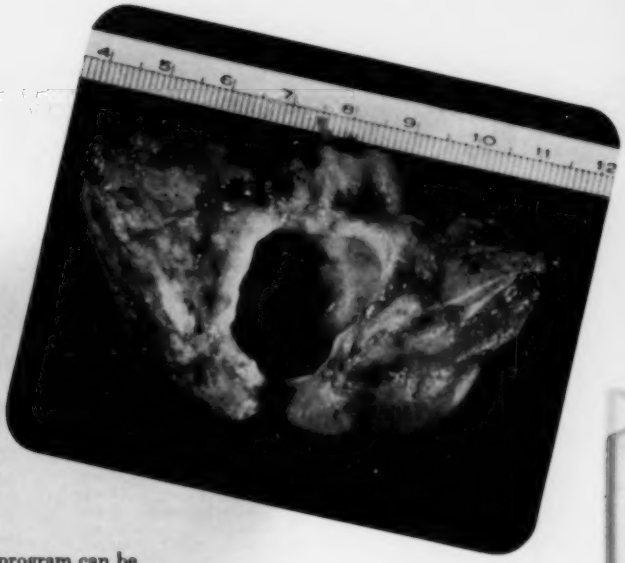

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OFFICIAL PUBLICATION

OF THE

AMERICAN COLLEGE OF CHEST PHYSICIANS

EXECUTIVE OFFICE
112 East Chestnut Street, Chicago 11, Illinois
MURRAY KORNFELD, *Managing Editor*

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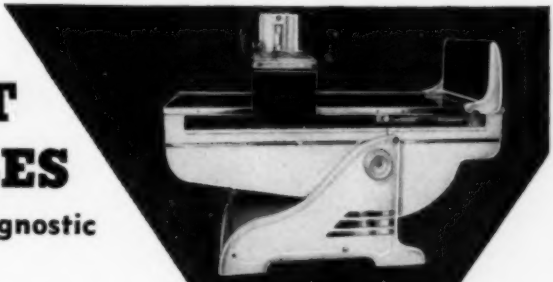

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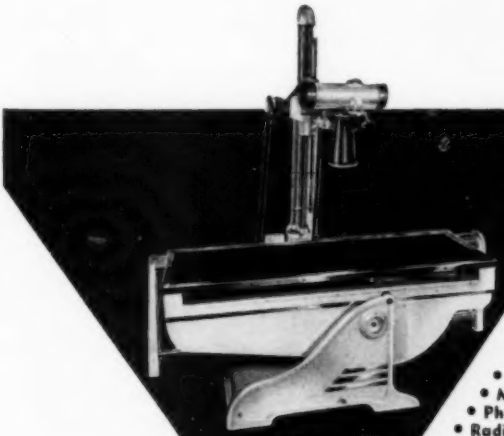

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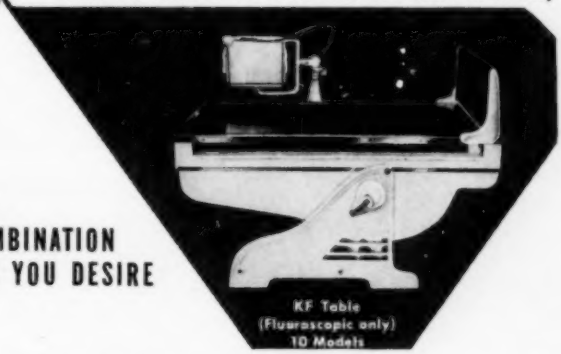

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XII Congress, International Union Against Tuberculosis
II International Congress on Diseases of the Chest
Rio de Janeiro, Brazil, August 24-30, 1952.

Intermin Session, American College of Chest Physicians,
Denver, Colorado, November 30, December 1, 1952.

19th Annual Meeting, American College of Chest Physicians,
Hotel New Yorker, New York, New York, May 28-31, 1953.

Chicago Postgraduate Course, October 6-10, 1952.

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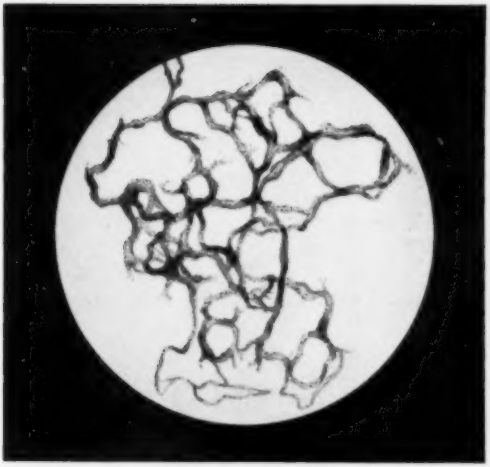

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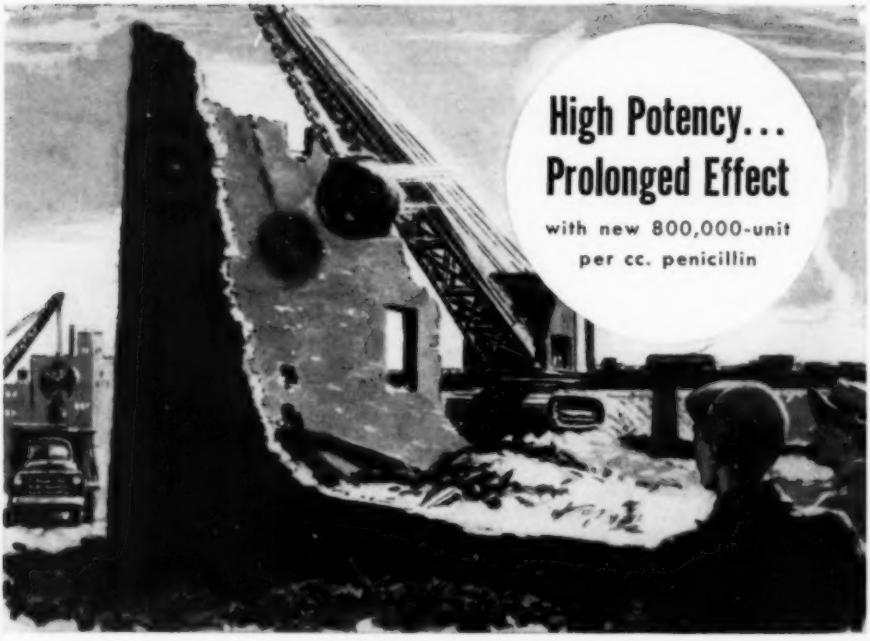

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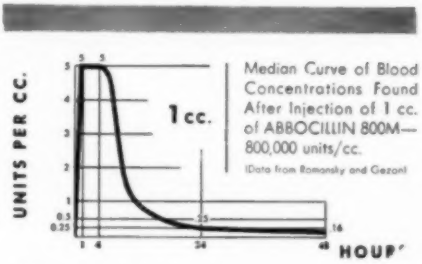

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DISEASES *of the* CHEST

VOLUME XXI JUNE 1952 NUMBER 6

Symposium on ACTH and Cortisone in Diseases of the Chest

Moderator: EDWIN R. LEVINE, M.D., F.C.C.P.
Chicago, Illinois

I would like to have the members of the panel come up and sit on the platform. I will introduce the members of the panel and then we will talk about the program.

Reading from me on the left, Dr. Laurance Kinsell of San Francisco; Dr. John Mote of Philadelphia; Dr. Smith Freeman of Chicago; Dr. Maurice Segal of Boston; and batting for Dr. Carlisle, who unfortunately was taken ill in Puerto Rico, we have the great good fortune to have Dr. Al Barach.

As you know, ACTH and cortisone have been discussed as much or more in the lay press than in scientific journals. Our patients know more about it than we do, and are sure that it will cure almost everything. Consequently, this subject is something that we are expected to know a great deal about. However, it is much too early to have much exact knowledge. We are finding that some of the concepts of the old clinicians of the last century about the body's reaction to disease are being corroborated on a truly physiologic basis since this work was started.

I am going to start by asking Dr. Smith Freeman to tell us what ACTH and Cortisone are and what may be the relationship of these substances to the functioning of the body in health and in disease.

Dr. Freeman: ACTH is a polypeptide that is liberated by the

Panel: Alvan L. Barach, M.D., F.C.C.P., New York, New York
Smith Freeman, M.D., Chicago, Illinois
Laurance W. Kinsell, M.D., San Francisco, California
John R. Mote, M.D., Philadelphia, Pennsylvania
Maurice S. Segal, M.D., F.C.C.P., Boston, Massachusetts

Presented at the Seventeenth Annual Meeting, American College of Chest Physicians, Atlantic City, New Jersey, June 8, 1951.

anterior lobe of the pituitary gland in response to stimulations which arise in various parts of the body and which presumably may be neurogenic or hormonal in origin. This polypeptide, with a molecular weight that has been given by various authors and workers as between 10,000 and 20,000, passes through the circulation and acts on the cortex of the adrenal gland to cause liberation of steroid hormones. It is a substance which is readily destroyed by proteolytic principals and its fate in the body is not known. For its function there must be an intact adrenal gland to respond to stimulation.

Cortisone is a steroid hormone; a specific substance with a definite chemical configuration which has its origin in the adrenal cortex and which acts on the periphery of the body, on the effector mechanisms to influence their response to metabolic stimuli. It does not require an intact adrenal gland for its function. It cannot be considered in all respects as producing effects synonymous to those produced by ACTH stimulation of the adrenal gland.

Dr. Levine: Dr. Kinsell, will you pick it up from there and tell us something about this stress or alarm reaction that we have heard about and how it relates to the body in health as well as in disease.

Dr. Kinsell: As all of you know, Dr. Selye is responsible for the term, alarm reaction. Over the past decade a great deal has been written and many theories presented concerning the role of the adrenal glands under various conditions, particularly emergency or stress conditions. In extremely brief terms Selye's concept of alarm reactions was that any individual subjected to a stress condition would have a reflex stimulation of the adrenals by way of his anterior pituitary, that is by means of the corticotropic hormone and the compounds poured out by the adrenals the individual would be helped to adjust himself to this difficult environmental situation. The same idea carried further by Dr. Selye, gave rise to his concept of the diseases of adaptation. If one accepts that concept and carries it through, he would place a great many conditions, such as hypertension and various forms of arterial disease in this category.

Dr. Freeman: A good deal of evidence has accumulated which indicates that every disease process probably provokes some sort of hormonal or endocrine readjustment to the disease process. The endocrine balance of the individual may be definitely altered by a disease even though the disease process may not be specifically or directly related to the endocrine system.

Dr. Levine: We now have developed the relationship which exists between stress or disease and the stimulation of the adrenal cortex by the corticotropic hormones of the anterior pituitary. Since

this may be the basis for the therapeutic usefulness of ACTH, I would like to ask Dr. Smith Freeman to tell us just what occurs when ACTH or cortisone is given to experimental animals or to human beings.

Dr. Freeman: ACTH must be given by injection because of destruction by proteotytic principals. It's not active orally. It should also be pointed out that the effectiveness of ACTH as regards adrenal stimulation depends upon the mode of administration, the frequency of administration, as well as the amount of the hormone administered. The same effect can be accomplished by much smaller doses given by continuous intravenous drip as by large injections given intermittently, whether subcutaneous or intramuscular.

We can't answer the question of how many hormones are liberated when the adrenal gland is stimulated. We can say that no single hormone has been isolated from the adrenal gland which in all respects will simulate the effects that can be produced by adrenal gland stimulation through the administration of ACTH. However, there are many metabolic effects in common from the administration of ACTH and cortisone. So what we will say now applies to both ACTH and cortisone administration.

When ACTH is given, it causes the adrenal gland to secrete. The response is almost immediate and the manifestations of this response can be demonstrated by changes in the composition of the blood. Eosinopenia develops which is maximal at the end of four hours and which is apparent before that time. Lymphopenia also tends to develop regularly which may be apparent in two hours. There is also leucocytosis with a shift to the left. There are also changes in the hormone content of the blood. Compound F is considered to be one hormone that is liberated by the adrenal gland. There may also be another hormone with a stronger effect on salt and water metabolisms as well as a hormone with androgenic activity.

The hormones have their effect peripherally on the tissues. They may affect the processes occurring in the liver. The tendency for protein to be converted into carbohydrate is augmented. The tendency for amino acids to be stored in the form of protein is suppressed. The mobilization of fat is augmented and the combustion of fat is increased. These are catabolic effects which affect carbohydrate, fat, and protein metabolism. At the same time there is a reduction in the peripheral utilization of carbohydrate. There may be changes in the renal threshhold, that is changes in the tendency for the renal tubule to reabsorb carbohydrate. Changes in the electrolyte metabolism also occur. There may be more tendency for sodium to be reabsorbed by the renal tubule and

less tendency for potassium to be reabsorbed by the renal tubule. The androgenic effects become apparent over a period of time. Changes in steroid excretion will also occur. Changes in the electrolyte composition of the blood are usually manifested by increase in the alkali reserve as reflected by the CO_2 content of the blood. The tendency for alkalosis to develop is one of the commonest manifestations of electrolyte imbalance, resulting from over stimulation of the adrenal cortex. There may be hypochloremia associated with this change or there may be an increase in the blood sodium with little or no change in the chloride content of the blood. Concomitantly and usually secondary to the development of the alkalosis there will be a reduction in the potassium content of the blood. This may be associated with weakness on the part of the patient.

The carbohydrate tolerance curve may be shifted towards that characteristic of the diabetic. Glycosuria may also develop in the patient. Hypertension may develop as well. And there may be some storage of water along with the storage of sodium. In addition to these specific effects there are the non-specific effects which Dr. Kinsell referred to. This is probably one of the most fundamental phases by which disease processes are altered, that is to say the body's response to injury is modified. The response to injury is suppressed and agents which under ordinary circumstances would cause marked cellular reaction with exudation and collagen elaboration no longer provoke that type of response.

Dr. Levine: At this stage of the game I think we ought to bring up the question of infection. We have been talking about reactions. Dr. Mote would you like to talk about the relationship of these substances to infections.

Dr. Mote: There has been a considerable amount of work done with ACTH and cortisone in animals and in human beings. This is one phase of experimental medicine where it would appear that the human being is your best experimental animal because of a number of real discrepancies between the results in animals and in human beings. Now to give an example in the question of infection.

Certainly most of the studies would indicate that the doses of ACTH and cortisone used in animal studies have if anything accelerated the course of the infection. It has spread more rapidly, the mortality rate has increased, and the duration of the experiment has shortened. Now that would indicate that they are both pretty serious hormones to use. Furthermore, in the experimental animal with the doses used of both hormones, there appears to be a suppression of the formation of antibodies.

Now let's switch to the human being. First I would like to say

that ACTH or cortisone, if the dose is sufficiently high, can and will do away with most or all of the symptoms of a great many illnesses, whether or not the course of the illness is altered. And that is also true of bacterial infections. Now you recall Max Finland treated lobar pneumococcal pneumonia with nothing except ACTH, and in the cases studied they recovered. It is interesting, that although all the symptoms of the disease disappeared in a matter of hours, the bacteria were still present and at least one case had pneumococcus septicemia with no symptoms whatever.

The other area, where it is important with regard to infection, is where patients have been on very large doses of either ACTH or cortisone. Here a bacterial infection can occur and not be detected at all, and the patients may be clinically perfectly well until suddenly they turn over and die. Fortunately that is usually on excessive doses of either hormone.

To give you examples, some patients with terminal carcinoma were treated with large doses of ACTH in Chicago by Taylor and Irons, and most of those patients were clinically well until shortly before death and yet when autopsies were performed they had extensive lesions, abscesses, pneumonic areas scattered throughout their lungs and elsewhere. And then you have McDermott's work in tuberculosis where he was looking primarily at the laryngeal lesions of tuberculosis which receeded rapidly under ACTH or cortisone and at the same time the symptoms and essentially most of the signs of the disease improved and some of the major symptoms disappeared entirely. So that I think you have a very real problem here. You have to use these things intelligently, and just because a patient doesn't do well at a given dose of either of them you can't make the assumption that you can go ahead and increase the dose. You may do away with all the symptoms and signs of intercurrent infection, although it is extending, and that's the danger, and that's why we have to be intelligent in their use and not overuse them. On the other hand, used properly, I don't believe the record is too bad for drastic things happening.

Dr. Levine: Talking about infection, let's go on with that. Dr. Segal, what's been your experience with ACTH and cortisone in infections?

Dr. Segal: I would like to talk about the use of ACTH in managing a group of patients with a large variety of pulmonary disease such as I have personally encountered. The danger of infection is really great and particularly runaway infection, once you begin to employ intravenous ACTH in particular. We made a cardinal rule of giving penicillin concomitantly with our use of ACTH in all patients who have any type of underlying pulmonary

pathology. Recently, we were treating a patient with ACTH in continuous intravenous form and he made a spectacular recovery from progressive pulmonary failure, secondary bronchial asthma, and emphysema. And while he was apparently recovering, approximately on the third day after having stopped the intravenous ACTH, he suddenly developed a temperature of 104 degrees F. with frank shaking chills and a great deal of cyanosis. We were unable to determine the cause of this high rise in temperature which persisted for four days. Blood cultures were negative. Widal, agglutinins, were all negative, and he recovered when high doses of penicillin were employed. He didn't respond to aureomycin. We have seen that this sort of thing occurs and in the early days with ACTH, particularly when the antibiotics were not used simultaneously. On the basis of our own observations, we now make a strict rule of giving penicillin along with ACTH.

Dr. Levine: What's been your experience, Dr. Barach?

Dr. Barach: In patients that have bronchial infections as demonstrated by pus cells in the sputum, either due to chronic bronchitis by itself or in association with pulmonary emphysema or bronchial asthma, we have observed increased suppuration in the lungs. These are cases treated for intractable bronchospasm. In one instance a patient discharged a yellow appearing material from the sinuses. It would appear that in those cases in which the choice had been made to use either ACTH or cortisone that an appropriate form of antibiotic therapy accompany the administration.

Dr. Levine: You said an appropriate form of antibiotic therapy. Dr. Segal mentioned penicillin, and he mentioned aureomycin. Would you then, Dr. Barach, use aureomycin and penicillin together or some such combination?

Dr. Barach: I wouldn't use aureomycin or terramycin or chloromycetin with penicillin. There is adequate evidence that these drugs should not be used together, for several reasons. The drug of choice, in my opinion, is penicillin. Certainly more gram positive organisms are found in bronchial infections. One may encounter a resistant staph in which one may use temporarily one of the other antibiotics. As a rule gram negative organisms do not primarily cause infection. They are regularly present after effective penicillin treatment for bronchial infection. Only rarely do they invade the lung. The most common is Friedlanders bacillus. When it is present then chloromycetin or terramycin or streptomycin may be used. There is considerable hazard in the attempt to eliminate both gram positive and gram negative bacteria. I don't think this is the place to discuss that because we are going to discuss that Monday morning. I would agree with Dr. Segal

that penicillin would be the first choice in all gram positive bacteria and only in the event that one has an actual proved case of Friedlander would one use any of the other antibiotics.

Dr. Levine: Dr. Kinsell, is there any reason to use either cortisone or ACTH in infectious processes in chest diseases?

Dr. Kinsell: I think there is a major use for ACTH and cortisone in many severe infections in the chest and elsewhere. Perhaps it would be well to just re-emphasize some of the things that have already been said. First that the adrenal steroids which result from ACTH administrations including cortisone and other things such as compound F do not exert any desirable effect in so far as bacterial growth is concerned. That is bacterial growth goes on at full speed and inhibition of growth is one of the things that they do not do. In the same breath, one can say in a broad and I think in a correct sense that ACTH and cortisone cure nothing. They have a multitude of effects but in terms of clinical thinking do not cure, particularly in regard to conditions which involve the chest.

Perhaps two positive effects deserve considerable emphasis. The one would be, that the adrenal steroids do apparently interpose a barrier between multiple toxins and multiple cells. So that in the case of Dr. Finland's pneumococcus pneumonia with bacteremia, the patient was clinically well despite the fact that he had flourishing bacteria in his blood stream. And one can make sense out of that by assuming this matter of the interposition of a blockade between the toxins elaborated by the bacteria and the body cells which previously had been badly damaged by the toxin. The second effect is that of production of lysis or prevention of formation of fibrous connective tissue. This can be either good or bad. In the case of chest conditions, obviously it can be bad. However, in the case of certain types of chest conditions, this may be desirable. I think that one can say that, if we for the moment leave out tuberculosis and some other granulomatous conditions, if we limit the consideration of ACTH and cortisone to the treatment of the more acute non-tuberculous infections.

In any patient who has a severe infectious process involving the chest which does not respond adequately to chemotherapy, the administration of adequate amounts of ACTH and/or cortisone, depending upon the particular situation, may very well be life saving. If a barrier can be interposed between the toxins and the organism, it will perhaps give the individual an opportunity to rouse and to mobilize his own specific defense machinery and give the chemotherapeutic agent a longer time in which to produce its effect.

Dr. Levine: Do we all agree on that? Dr. Kinsell has suggested

a method of approach in severe infections which would seem to depend on a delicate balance. Dr. Mote, what do you think of it?

Dr. Mote: I am sure there would be considerable difference of opinion on Dr. Kinsell's last point. And I think it will take considerably more work before there will be unnanimity of opinion on either side of the fence. We really don't know enough about this barrier that he speaks of, as to how much of it is good and how much of it is bad. And of course this is just one of the minor details. Briefly you might say that this is a new era of medicine and the greatest challenge of modern medicine. And don't be surprised if you see conflicting reports coming out because no one known any of the answers just yet. It will require a considerable amount of experimental work over the next decade before all the answers are clear cut.

Dr. Levine. A question has just come from the floor. It relates to an effect produced by long continued usage of ACTH. In the particular case mentioned, a male of 55, who was on continued ACTH therapy, suffered marked and disturbing loss of libido. Dr. Freeman, does this occur commonly in patients under such treatment?

Dr. Freeman: Loss of libido occurs frequently in the male. Of course you have to qualify this statement because a number of males who have been sick and unable to have many ideas, have gotten rather strenuous ideas, and conversely I quite agree that some of the males certainly lose their libido. Likewise some women have increased libido and some not.

Dr. Segal: The oldest man of our series was 72. And on the other hand he had his first successful erection and emission following a complete remission of status asthma after a successful course of ACTH.

Dr. Levine: We have a question from the floor, which may be related to the same subject. It is in regard to a patient who was receiving ACTH in large doses. One day he offered to buy the doctor's wife a cadillac car and rapidly showed other signs of euphoria and grandiose ideas. What is the relation of euphoria and ACTH treatment? Now who wants to answer that one? Dr. Mote is going to try it.

Dr. Mote: I said I'd try it. As you may know, there have been some studies concerning the electroencephalographic recording of people on ACTH. I'm not an electroencephalographic expert, but there certainly has been an increased amplitude. Some people have thought that what you really are doing is raising the pitch or mental activity and allowing fundamental problems, that you otherwise keep repressed, to come to the top and up to the conscious level. Actually, no one has studied this problem of behavior

patterns in sufficient detail to know all the answers. It poses an intriguing problem, and it gives some insight into what makes successful businessmen and other people like that. Maybe they have a sensitive adrenal pituitary mechanism. It certainly needs investigation. I'm sorry you didn't get your cadillac.

Dr. Freeman: There are a few other considerations that might have a bearing on the cause of the euphoria. Usually these patients manifest some euphoria which may be physiological in origin. Later on they may have insomnia and then may become frankly psychotic in some instances. Usually at the time when these manifestations become apparent there are frank disturbances in electrolyte and carbohydrate metabolism. Maybe not invariably but frequently this is the case. The combustion of carbohydrate is exclusively the source of energy for the brain, and since the peripheral utilization of carbohydrate is modified by hormonal balance, there is a definite possibility that the utilization of carbohydrate by the brain may likewise be modified or reduced to some extent in relation to the hormone balance brought about by the therapy.

The second possibility is that a redistribution of electrolytes in nervous tissue may be brought about by hyperfunction of the adrenal cortex. An increase in sodium content of the cell, and a reduction of potassium content of the cell takes place in an alkalosis and in response to adrenal hyperfunction. I have also seen psychotic manifestations in patients that have undergone electrolyte depletion when they have been maintained on a low sodium diet or on an acidotic regime for a continued period of time. So I think redistribution of electrolytes might be a factor.

Dr. Levine: Now let's discuss the clinical use of ACTH and cortisone. Dr. Segal, would you like to discuss bronchospastic diseases with particular emphasis to asthma.

Dr. Segal: The patient with serious bronchial asthma, in the status state, presents a difficult and important therapeutic challenge. In this group of patients, ACTH and cortisone offer an effective way, in a good percentage of them, of inducing a remission. These remissions, unfortunately, are brief in duration. They may last varied periods of time, from days or weeks up to several months or perhaps longer in the occasional patient. Repeated courses of therapy may be necessary and six to seven or eight courses of therapy in a period of a year have been given to some of these patients. There is the law of diminishing returns, usually with repeated courses of therapy. The good effects one sees in the first or second administration are not seen again subsequently. We have given approximately 75 courses of therapy and have been rather encouraged at the immediate results fol-

lowing such therapy. Certainly it is an important adjunct along with our physiologically directed therapy. We seldom treat patients with ACTH in severe asthma.

It's generally our custom to set up a continuous intravenous drip of 5 per cent glucose in distilled water, giving three liters in a 24 hour period, accomplishing this by a flow of 30 drops a minute. We add aminophyllin in various concentrations to the intravenous infusions. And then in our very next period we employ ACTH parenterally and to save time we are also employing ACTH in continuous intravenous drip, but more about that later.

We are not able to demonstrate in these cases any reversibility of the antigen antibody mechanism. We don't see any consistent changes in skin tests. We haven't been able to show any changes in passive transference and we have not been able to show in the acute asthmatic patient any block in the effects of histomines or acetylmethylcholine. On the other hand, we have been able to show a protective block against the effect of dog dander or feathers in particular cases involved.

Dr. Levine: Dr. Barach, do you want to pick it up there and tell us how you decide, in the treatment of the asthmatic patient, when to use ACTH or cortisone, and also something about the management of the case under such treatment.

Dr. Barach: My impressions are based on 60 patients who have had either bronchial asthma or bronchospastic type of pulmonary emphysema. These patients have received a total of 120 courses of treatment. In 20 courses, about 16 per cent, ACTH or cortisone appeared to serve a useful purpose. In 12 of these the duration of the improvement was longer than two months.

There are certain groups of people that I think may be benefited by cortisone or ACTH and there are others we have studied who, I think, are not benefited. The ideal patient has bronchial asthma due to ragweed pollen, who is in some general hospital with severe asthma on about the 15th or the 20th of September, where you know that with the first frost the asthma will be over. We have treated several such patients either during the summer or the late summer. That in a sense is a self-limiting disease. The use of ACTH or cortisone under those circumstances gives a period of remission, the average of which is about 19 days, long enough to carry through the ragweed season. There is another group of cases in which the patient with bronchial asthma has not been in bad shape but after a couple of respiratory infections begins to have severe attacks. Some of these cases have done well on ACTH. On the other hand, patients with intractable bronchial asthma, in which there is no obvious precipitating cause, are not

benefitted by ACTH or cortisone except temporarily. In these cases, our regular experience with ACTH is the swift law of diminishing returns. The third course, repeated after a week, may be of little help. Our belief is that in the treatment of any of this group of cases, if we find a reason and can look forward to eliminating the cause, we will get much better results. Such a situation may be the termination of pollen or the interruption of the intractible cycle due to colds or to prepare the patient for some other kind of procedure such as pneumoperitoneum or to teach diaphragmatic breathing, or some other kind of help that will carry on where the ACTH leaves off. We are on far firmer ground if we treat patients with intractible bronchospasms of the type that does not go from one seige into another.

In our early series we had two cases of edema of the lungs on ACTH. It often is rather difficult to tell if the patient with severe asthma has circulatory insufficiency. But it is desirable in these cases to give three grams of potassium chloride a day for the reason that if we do find moist rales developing in the lung we then give mercuhydrin, preferable on the third or fifth day of treatment. If you haven't given potassium chloride and then give mercuhydrin, you will not only get a loss of sodium but acute potassium deficit with weakness. Giving potassium is desirable even though the serum potassium level may be unchanged. Potassium is lost in the urine, and we do not have an adequate method of measuring this except by the electrocardiogram. So we are in a better state of protecting the patient from possible complication if we have given potassium chloride, and then mercuhydrin freely.

I've had this experience a number of times that although moderate doses of either cortisone or ACTH would get a good many people free of symptoms, there are also many more cases of asthma or bronchospastic emphysema in whom one may give a 160 or 200 mg. of cortisone a day for 10 days without any result. We have simply wasted the patient's time. We are better off if we give a large dosage to almost every patient. I also have the feeling that the remissions are longer. By a large dose I mean giving cortisone at 400 mg. a day in divided doses for a period of three to four days and 300 mg. a day for sometime more. With ACTH I like to begin with 50 mg. every six hours round the 24 hours. Under those circumstances the remission takes place fast. On the third day the remission is secure and steady. And if there is something in this separation of the antigen and the antibody in asthma, then a longer period of freedom is obtained. One must watch the weight, maintain a rigid low salt diet, and potassium chloride must be given. There is no harm in these large doses, since far larger doses than these have been given. The same

applies to cortisone given intramuscularly. In those cases we realize the problem has been a severe one.

The side effects of the drugs are not so apt to take place with a limited short dosage of four or five days with ACTH and eight days with cortisone as they are naturally with the longer periods of treatment that are used in arthritis. In our cases there have been no serious mental effects. We have observed the usual well being. In only one case a woman was depressed, and this was because she wasn't elated as she had hoped to be.

Dr. Levine: Dr. Barach's discussion of the clinical problem represented by the sodium and potassium levels brings us back to our previous mention of the metabolic effects of these substances. You will remember that among the effects produced are changes in the carbohydrate, fat, and protein metabolism. In addition there are changes in the renal tubule which results in a greater tendency for sodium to be reabsorbed and a decrease in reabsorption of potassium. All of this brings up questions of proper management of the patient under treatment. First of these is what are the laboratory tests essential to the management of the patient receiving one of these drugs. Dr. Kinsell, would you like to give us your opinion?

Dr. Kinsell: I'd be glad to, and I'd like to respectfully disagree to some extent with the management of asthma, from one standpoint only. I agree thoroughly that the initial administration of large amounts of hormones in asthma and in most other chronic conditions represents an optimal procedure. Gradual reduction in the dosage, and in the case of most patients with asthma the following of the eosinophile level, is apt to be a helpful procedure. In the allergic states, particularly, the level of the circulating eosinophiles is apt to coincide precisely with the clinical status and with the degree of therapeutic effectiveness of the hormone. Our experience with asthma is not nearly as broad as that of the previous speaker, but all of the patients whom we have treated or have followed have been known to have severe asthma of many years duration. Asthma which has received every kind of treatment in the book without benefit. And it is our strong feeling that continued treatment without interruption with gradual reduction in dosage will produce a better result in the long pull than will intermittent therapy. That is recurrent courses of therapy. This statement applies only to the severe intractible asthmas with long duration.

Now as to the basic laboratory and physical things that one follows in terms of evaluation of the patient and in terms of keeping him in the best possible clinical condition and in terms of obviating or eliminating completely or nearly completely any

of the untoward effects of ACTH and cortisone. First, every patient under treatment, at least in the early phases and preferably longer, should be weighed every day. If the body weight is increasing rapidly, it may indicate fast fluid accumulation. And by the same token, the dialy checking of the blood pressure in patients who are home should be done. One can perfectly well arrange for a visiting nurse or even a member of the family to do this to save the patient expense and to save the doctor unnecessary trips. Second, an initial base line before any treatment is instituted should be obtained. There should be at least two fasting blood sugars and two eosinophile counts. The vast majority of patients who receive ACTH and cortisone will not get into trouble in so far as their carbohydrate metabolism is concerned. There's no question that all of us will, in the years ahead, tend to precipitate diabetes in people who are in a rather diabetic state. For that reason, it is most essential that one know what the fasting blood is prior to therapy and that the sugar be followed at intervals of two or three times a week in the first week or two of therapy and then at gradually decreasing intervals. Slight elevation is apt to occur, but if this is increasing one needs to take heed.

The evaluation of the eosinophilic count, preferably by the Randolph technique, is a simple procedure and a valuable one. In the case of ACTH it tells one whether the particular individual has adrenals which are responding to ACTH in adequate degrees. This can be used as a diagnostic procedure of adrenal insufficiency. In terms of therapeutic evaluation, by and large, one tends to keep an eosinophile count at least in the early phases of therapy, below a level of 100 per cubic mm. Many of the asthmatics and patients with other allergic states will have initial counts which are up in the thousands. The normal range varies from 150 to 250 per cubic mm. With adequate therapy in patients with high eosinophile counts, there will be a fall to zero within the first two days of treatment. To obtain this effect one needs to use about 25 mg. of ACTH intramuscularly every six hours, that is 100 mg. a day, or in terms of the continuous intravenous infusion somewhere between 10 to 40 mg. a day, depending upon the patient. With cortisone, the dose may be as much as 600 mgm. in the first day or two, but usually 300 to 400 mgm. will be adequate to produce this desired depression in the circulating eosinophiles.

The matter or routine limitation of sodium and the routine administration of large amounts of protein is most essential. One of the outstanding effects of large amounts of these hormones is the catabolism that breaks down body proteins, so that one wants to supply large amounts of dietary protein, that is in excess

of 120 grams per day of good, biologically adequate, protein and to limit the sodium intake to a low figure. What may be considered a low figure varies among individuals. In some people, particularly those who have any tendency to hypertension or to abnormal fluid accumulation on a cardiac or other basis, it will probably be necessary to limit the sodium intake to less than 300 mgm. daily.

To combine a high protein intake with that low a sodium intake means that one has to use special preparations. A very satisfactory one which we have used and are using to a great degree is one of the reconstituted desalted milk preparations. By using this as a dietary supplement one can increase protein and still keep the sodium low. To administer supplemental potassium, the simplest form is the saturated solution of potassium chloride given in such an amount that the patient receives in the neighborhood of 4 to 6 grams of potassium chloride a day. It is not well to monkey with homeopathic doses. If the patient has any renal insufficiency, then obviously one is careful both about the addition of potassium and the addition of protein. But in the presence of normal renal function, one may safely administer such amounts of potassium.

One other item is the co-administration of testosterone. Reverting to previous discussions, but not with that particular concept in mind, testosterone has the opposite effect of cortisone—like adrenal steroids in that it is a powerful protein anabolic agent. It causes the building up of protein tissues. If one gives a sufficient amount of testosterone, one not only conserves protein and neutralizes the protein catabolic effect of ACTH and cortisone to a large degree or completely, but he also specifically conserves potassium and also tends to put it where it's needed, which is inside the cell. One could go on at great length within terms of intravenous potassium administration under acute conditions, but those are at least some of the essentials relating to the medical management of these patients.

Dr. Levine: That sounds to me as though the use of this material isn't exactly routine office practice. I would like the various members of the panel now, running right down the table, just to take a few minutes and state whether they agree that all this work-up is necessary, or, on the other hand, if something has been left out—and just what are the measures that you think ought to be used in control of the patient under treatment.

Dr. Mote: Dr. Kinsell's outline reflects his training. He happens to be a metabolic man. It's certainly true that in certain situations one may need all of the things which he mentioned. None the less I would say that to try to keep all of those in mind in an office practice would be nearly impossible. My personal view would

be first to check the eosinophils. Second the electrocardiogram periodically every couple of weeks. Third, I would protect the potassium situation of the patient by giving liberal potassium. And fourth, I would restrict sodium intake to no added salt if you are on a regular salt diet.

Again if you are going to work with all high doses of ACTH or cortisone, I agree with him that this business of carbohydrates is something to take into account. But under the ordinary circumstances I'm not at all convinced, on the data I've seen to date, that that is a real threat. I haven't been convinced that one can cause true diabetes by cortisone or ACTH. You can cause glycosuria and hyperglycemia in some cases. In other words, unless one is working with high doses, the management isn't as difficult and does not require as many studies. From a straight clinical point of view, daily weight and blood pressure, in the beginning until the patient is stabilized, is in order.

Dr. Freeman: The initial work-up should be in a hospital. The major items have been indicated by Dr. Kinsell. The tests are really divided into two groups; those that have to do with the evaluation of the therapeutic effectiveness and those that have to do with toxicity.

The initial development of eosinopenia is one of the best laboratory guides as to the adequacy of the dosage of hormone. It indicates that the ACTH is producing a decided stimulation of the adrenal gland or that the amount of cortisone administered is enough to produce this reaction. Then the therapeutic objective becomes to utilize the minimal dose of the hormone which will bring about the desired effect clinically.

As part of this first hospital study we have carbohydrate tolerance and the other things that have already been mentioned. I think the electrocardiographic tracing should also be included in the preliminary study as it may be a valuable aid later on as an indication of the electrolyte inbalance or depletion, and for interpretation of any complication that may arise in the course of therapy. After the patient has had a preliminary study a clinical dosage schedule is initiated and then the dose is tapered to the minimal level for effective therapy. There will have to be routine check-ups after the individual has gone home every week or so until the clinical response is thoroughly established.

What is the minimal dosage that can be used in the management of the chronic patient? The amount is variable and quite unpredictable in a given instance. I remember one patient with pulmonary tuberculosis who developed diabetes so far as carbohydrate tolerance and glycosuria were concerned on 40 mg. of ACTH daily, and this glycosuria and some of the hyperglycemia

persisted for a month after therapy had been discontinued. In other patients I have seen a prediabetic carbohydrate tolerance curve prior to the time of ACTH administration, which was not influenced at all by the administration of fairly large doses of ACTH. So one can make few generalizations about the response of the patient.

We have to realize that the frequency of administration of the hormone is related to the effectiveness of any given dose. And that various nutritional states of the patient may also influence his response to therapy. Debilitated, undernourished individuals give a poor response to ACTH. They usually have a low ketosteroid excretion and other evidences of reduced adrenal function, and they may be slow in their response to treatment as evidenced either by steroid excretion in the urine or by the eosinopenia produced by the hormone. The range of dosage which we have found compatible with chronic therapy has usually been around 20 to 30 mgm. of ACTH daily given in two to three doses. We have seen few patients who could tolerate more than 30 mg. daily for an indefinite period. We have one chronic asthmatic with recurrent episodes of status asthmaticus who has tolerated 40 mg. daily in two doses over a period of six months. We have a few patients that have taken 20 to 30 mg. a day for over two years.

Dr. Segal: It's differences in opinion that has always made horse races popular. We have been disappointed in continuous therapy in bronchospastic disorders. After our preliminary investigations, we have made a rule of treating our patients from three to 19 days with intensive therapy and then carrying on maintainence therapy with rectal aminophyllin and effective bronchodilator drugs and other supportive therapy. We resort to repeated courses of therapy rather than protracted continuous courses. We see a high incidence of refractory asthma that does not improve with continuous daily ACTH therapy. We have studied eight such people. When they came back in severe status asthmaticus we resorted to continuous intravenous therapy. In spite of the inconvenience of administration of this therapy one has a real opportunity of sending an infant on a man's errand. The doses are small. We employ a continuous 24 hour drip technique in contrast to the eight hour technique suggested by Thorne and Gordon and others. We give 10 mg. of ACTH to each liter of solution of 5 per cent glucose in distilled water and use three such liters per day. We have noted that in patients with refractory asthma, the eosinophile count comes down strikingly within a 24 hour period.

Studies of metabolic function are indicated and are of great interest and value in the patient treated for any considerable period of time. We routinely give six or eight ounces of orange

juice every morning to all our patients and that's quite a valuable amount of potassium. In addition, we give potassium iodide in dosages of 15 to 20 minims every four hours, and we feel that takes care of their potassium need. We're not particularly concerned about their potassium need except on the intravenous route of administration. We restrict salt, and should call attention to the danger of the high sodium content in the drinking water of some cities.

Dr. Barach: I think it is good to bear in mind that bronchial asthma can be treated by other means than either ACTH or cortisone. It is a disease in many instances of food or allergic origin in which removal or control of the precipitating factor may be of value or other forms of remissive therapy can be used. I advise against continuous treatment with the substances under discussion over a long period in patients with asthma. Those I have seen on such treatment for two months in bed are unhappy and not well. The longer we give ACTH the more we are apt to run into allergic reactions, diabetes, etc., and must take precautions necessary to prevent hypertension, cardiac insufficiency, and protein loss. Asthma is a disease of a paroxysmal nature, and I would doubt very much that it is necessary to give long courses of ACTH. If we do, then we run into hazards that often make us wish the drug hadn't been used. All of the conditions associated with asthma can be met with or coped with, in brief courses of either ACTH or cortisone.

Dr. Levine: Now a question has been asked from the floor on an entirely different subject. Have cortisone or ACTH any value in the treatment of sarcoidosis? Who wants to answer that? Dr. Mote?

Dr. Mote: There are some studies being reported at one of the meetings this week in which large doses of ACTH have caused marked regression of sarcoid lesions. It was first observed about two years ago in a case of sarcoid of the eye. It wasn't taken too seriously, although the eye lesion cleared up. The work was not followed up for a matter of a year and a half. It certainly requires large doses and it is too early to know how soon and to what extent the disease will recur. With lesser doses it has not been satisfactory and recurrence has been rapid. With larger doses it appears to be most encouraging.

Dr. Levine: The next question. We've heard a lot about the danger of using ACTH or cortisone in the presence of infection, and that of course would include tuberculosis. Is it safe to use ACTH or cortisone in a patient who has fibroid or apparently healed tuberculosis? Dr. Kinsell.

Dr. Kinsell: One has to assume that any patient who has had

tuberculous infection is potentially in line for activation of that infection if he receives long term ACTH and cortisone therapy. And further when one adds to that the ability of ACTH and cortisone to mask even advanced and advancing pathology, it means that he has to constantly be on guard in any patient on long term maintainence therapy. I don't think there is any question that inactive processes have already been lighted up in quite a number of people. There is no question that many more will be. Precisely what the answer may be to this I don't believe that anyone knows. Fortunately it is not a usual or a common occurrence, but it can happen and does happen.

Dr. Levine: Having heard so much about the danger of tuberculosis and ACTH, it occurred to me that those who are treating so much arthritis should have gotten into trouble with their patients in the older age group in which we are finding so much evidence of tuberculosis. I spoke to one man who has probably treated as much arthritis as anybody in the country and asked him how many cases of tuberculosis had developed, and he said, "What do you mean cases of tuberculosis, we haven't had any." I took occasion to look over a group of his x-ray films, and he had a percentage of nodules that were very obvious in some of the films but apparently none of these people had developed active disease. Has anybody here an opinion of how much activity or potential activity of tuberculosis would seem to be necessary before there is real danger in the use of ACTH or cortisone?

Dr. Mote: I can only tell you what I know, and what I've heard. There are cases under treatment who have had recent tuberculosis that have frankly broken down. Two of them with almost disasterous effects because there were no symptoms or signs. A bit of a cough but no fever, nothing in the way of symptoms until an x-ray film was taken and a complete consolidation of one lung found. It turned out to be tuberculous. Now on the other hand, there have been to my knowledge old well healed lesions treated and I don't recall any of long standing cures that have flared up. I agree with Dr. Kinsell, theoretically, that it's possible. A patient who has had recent tuberculosis should be watched carefully when using either hormone. If one has to use them one ought to accompany this treatment with adequate doses of antibiotics. Always keep in mind that one can completely mask the flare-up if it should occur. But it doesn't appear at this time to be a real danger in old, well healed cases.

Dr. Levine: Of course it's a nice thing to know if the tuberculosis is well healed. How often does coronary thrombosis occur in elderly patients treated with ACTH and associated with that question on the incidence of thrombo-embolic phenomena during

treatment. Dr. Freeman, would you like to answer that question?

Dr. Freeman: Well, we have had one or two arthritic patients who had coronaries while under treatment with ACTH. One man who had been on treatment for about one and a half years had a coronary and there have been several instances of thromboembolic phenomena reported. However, there hasn't been any clear cut evidence that there was a close association between the use of these agents and the development of these changes.

Dr. Mote: Of course one will have to keep in mind that many diseases affected by ACTH and cortisone are rather prominent in the age groups where they have arteriosclerosis and coronary disease. I don't believe there are any statistics that would indicate a direct connection, but there have been some cases of coronary disease develope while patients were on ACTH or cortisone. At the same time with this treatment, we have taken bed ridden patients and given many of them the chance to live a normal life. I think we have to keep in mind that we are in an age group where these diseases occur. Thromboembolic phenomena have been reported, on the other hand, we have groups supporting the use of the hormones in the treatment of thrombophlebitis. So we have it at both ends. That is an interesting thing about this period in medicine. We can have apparently completely contradictory results which in some cases are perfectly valid observations. It just simply shows how little we know.

Dr. Segal: We know little about these drugs and I am rather curious to see if someone on the floor would ask how these work. They cure nothing, but make a lot of people feel well. The only data we have is that they probably throw up a protective barrier around the cell, protecting it against a wide variety of stress and stimulae. I should like to ask any member of the panel to tell us what is going on inside the cell.

Dr. Mote: I'd love to tackle that one. We talk about this barrier that is set up by the cell. The thing we have to be most careful about is not so much the barrier in that cell but rather an intellectual barrier that this tremendous challenge has thrown up and the terrific amount of imagination that will be required to rationalize any of these problems. Before it is all over we will have a great many new concepts of medicine, a great many new concepts of disease, a great many new concepts of teaching, and I am afraid it will be several decades that we must guard against building up an intellectual barrier at facing what appears to be an insurmountable intellectual challenge.

Dr. Levine: Will insulin control the effect of ACTH on carbohydrate metabolism in a moderate diabetic, especially with reference to brain damage?

Dr. Kinsell: We have, with malice aforethought but under carefully controlled experimental conditions, used ACTH in some mild diabetics under study of the metabolic ward. I think one can answer that question best or most briefly by saying first the diabeticogenic effects of adrenal steroids is associated with insulin resistence. That is if one takes a given diabetic patient who has had an insulin requirement, say of 10 units on a given diet and keeping everything constant, administers increasing amounts of cortisone or increasing amounts of ACTH to that patient, the insulin requirement will go up in a manner which suggests a geometrical progression type of affair. If the dosage of ACTH is sufficiently large, as much as several thousand units of insulin a day, and that is an actual occurrence, may be required to control the diabetic state. When such hormone administration is stopped, in the space of a short time the diabetes tends to go back to its original state. The co-administration of insulin, however, is mandatory if one must give ACTH or cortisone to a diabetic patient because of some condition which endangers his life and in which one has a good reason to believe that the hormones may be of real value.

Dr. Levine: If a patient who is receiving ACTH develops a hemorrhage from a gastric or duodenal ulcer, would you say that this was due to the use of this substance?

Dr. Segal: I think a group of investigators, Dr. Graham in particular, have conclusively shown that there is an increase in lipo enzyme titre with ACTH therapy. Therefore, one should always, before using ACTH or cortisone, get an accurate history to be sure that there is not a peptic ulcer and that one did not exist. There has been an increasing number of blow-outs, perforations, and hemorrhage on this therapy in such cases. I personally have not encountered any.

Dr. Levine: What determines whether to use ACTH or cortisone?

Dr. Barach: That is a difficult question to answer. It depends on several considerations. I don't know if I am in a position now to state my preference for either ACTH or cortisone. I don't think I have enough data to make whatever opinion I have valid, and I would just as soon pass it on to someone else. I would like to add one thing however. We have had three allergic reactions to ACTH, two of them very alarming. There was acute anxiety and difficulty in breathing taking place within a very short time after intramuscular injection of ACTH on the second course. In each instance intravenous benadryl seemed to be far more valuable than the previous injection of adrenalin. From the safety point of view as far as I know no such reaction has taken place with cortisone, or have they?

Dr. Mote: I must say it surprised me, but there have been two definite cases of marked allergic reaction to cortisone and I don't understand it anymore than anyone else does, because it's certainly not common to have an allergic reaction to steroids. Both of these were where cortisone was injected, not taken by mouth.

Dr. Levine: I think that we can continue with this discussion for quite a little while. There is a great deal to discuss and many questions can be raised, since there is certainly not enough definite information on either substance, how it affects the body or how the body reacts to disease, to stress, to disturbances of many kinds, to permit anyone to make definitive statements.

Since it is necessary to draw the symposium to a close, let us try to summarize what has been discussed this afternoon. First let us accept the fact that with the introduction of these two substances, ACTH and cortisone, we are entering a new stage in the study and treatment of disease. It is the field of attempting to change the reaction of the body to a disease process rather than the attempt to attack the disease itself.

As regards the two new substances in question, it must be remembered that although their effect as measured by end results may be much the same they are different and their mode of action is different.

ACTH is a polypeptide liberated by the anterior lobe of the pituitary gland and which acts on the cortex of the adrenal gland to cause production or liberation of steroid hormones.

Cortisone is a steroid hormone itself which has its origin in the adrenal cortex and acts on the periphery of the body.

ACTH requires an intact adrenal cortex if it is to be effective, whereas cortisone is a substitution product and thus does not require an intact adrenal. Cortisone for all practical purposes produces similar results to those created by stimulation of the adrenal gland by ACTH.

In the use of these drugs there are many and profound changes occurring in the body which must be remembered, measured, and in some cases compensated for, if therapy is to benefit the patient. Consequently, a patient who really needs ACTH or cortisone therapy should always be hospitalized at least in the early part of treatment. During this period the patient should be weighed every day to detect early rapid fluid accumulation. Likewise blood pressure should be checked and a baseline of blood sugar and eosinophil counts should be made. In general, sodium intake should be limited, the protein intake increased, and supplemental potassium should be given.

As regards clinical use, to date it has been found most effective in asthma, Loefler's syndrome, and possibly Boecks sarcoid.

Whether there is any application to tuberculosis is yet to be determined. Thus far the evidence points to a deleterious effect on the disease while the patient feels improved. There is some suggestion that methods of its utilization may be found and the substances applied to emphysema, pulmonary fibrosis, and interstitial pneumonitis. In bronchogenic carcinoma, although the disease as such is not involved and its course remains unchanged, the condition of the patient may be sufficiently improved to justify its use.

Certain dangers must be borne in mind. First, the development of severe diabetes in individuals who might be considered prediabetic. Second, the chance of infection developing and getting entirely out of hand before it is recognized, and third, that allergic phenomena may be caused by ACTH as well as relieved by it.

The dosage will vary with the individual and the type of case treated, it being a good rule to use the lowest dosage that will produce the adequate results. There is some difference of opinion as to whether long term continuous therapy is more desirable than repeated courses of more intensive treatment.

With these few highlights let us close our discussion by saying the panel today has given us a view of the basic information and experimental background of ACTH and cortisone and some insight into its mode of action, method of using, and possible use for the future. I cannot remember where a subject involving both laboratory investigation and clinical experience has been so well and so clearly discussed. I should like to thank the members of this panel for their discussions and to compliment them on a job well done.

Precordial Migraine

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Migraine is not an unusual or uncommon condition. The frequency with which it is seen varies according to the type of practice of medicine, as well as to an inherent interest in the subject of migraine. This condition may be defined as a periodic, recurring type of headache of unknown cause occurring in otherwise normal people. These headaches are usually associated with gastro-intestinal as well as ocular symptoms. The etiology of this syndrome still remains unknown. There is definitely a hereditary and familial aspect to migraine, and many factors have been put forth in an attempt to explain the recurrence of the headache. At some time or other, such things as allergies, emotional upsets, and the like have been suggested as the probable cause of the migraine attack. There is, however, no adequate explanation as to why patients have these seizures.

The disease apparently is more common in women than in men, and it often stops at the time of the menopause. At least, the seizures are less severe following the menopause.

Migraine seizures not only have associated ocular and gastro-intestinal symptoms but many other organ groups in the body may be involved in the migrainous attack, so that the patient will have not only his migrainous seizures, but he may also have distress in various other parts of his body. Further, during the migraine episode, the patient may suffer from periods of agitation somewhat suggestive of psychomotor epileptic attacks. Upon occasion, definite neurologic signs and symptoms may develop during the attack. In addition, patients have been known to have signs and symptoms indicative of renal colic concomitant to their migrainous episode. The migraine individual may have a head pain of such severity that it overshadows any associated organ symptoms. On the other hand, it is possible for the patient to have an attack with violent distress in various organs of the body with the head pain absent or of such slight degree that the patient overlooks the presence of his headache. Thus, it becomes possible for other organ groups in the body to take over the predominant clinical picture in the migrainous seizure. This will then result

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in what we term a migraine equivalent; thus we may speak of abdominal or cardiac rather than a cephalgic migraine.

The mechanism that produces the pain apparently is the result of distension of the cranial arteries. At times, this may be so severe as to involve the external carotid and its branches. Further, as a result of the sustained contraction of the muscles about the head and neck, a pain of muscular origin may predominate the clinical picture, and this pain of muscular origin may persist long after the headache has disappeared. The prodromal appearance of visual disturbances in people with migraine, such as scotomata and the like, usually represents an initial cerebro-vascular constriction and this is then followed by a period of vasodilatation. One of the important factors in both the diagnosis and treatment of patients is to recognize the importance of the psychological factor. Numerous studies have demonstrated that a great many of these patients are usually perfectionistic individuals inclined to great resentment and frustration; and also are very anxious people. It is the handling of the common personality background that is so important in the treatment of patients with this disease. Often, the initiating mechanism for the headache may be minor, but because of the nervous temperament of the individual, the seizures may be severe.

Precordial Migraine

One of the unusual variants in patients with migraine is the presence of precordial distress. Little has been written about this particular type, nor has it been emphasized too often that upon occasion the precordial features of the seizure may mask the cephalgic nature of the attack to such an extent that the migrainous nature of the precordial pain is overlooked. It is worse, however, when the patient develops severe precordial distress as the only manifestation of his migrainous attack. Because of the very nature of the precordial pain and its symptomatology, the picture may often suggest organic heart disease.

Precordial migraine has been known for many years. Wartenberg writing on the Neurology of Bing, states that in a discussion of migraine Bing mentions that there are migraine equivalents which consist of vasomotor angina pectoris. Bing also mentions that pain may occur in the arm as part of the vasomotor disturbance associated with a migrainous attack. Donahue mentions the existence of precordial migraine in his report on Migraine and Its Ocular Manifestations. Wolff, in writing about migraine mentions that among the migraine equivalents, is pain localized in the thorax. The history sheet used at the Montefiore Hospital by the physicians of the headache clinic have listed under migraine

equivalent a place for precordial pain, thus recognizing also the existence of this form of distress as an equivalent to migraine. Fitz-Hugh, has made an excellent review of the problem of precordial migraine in which he emphasizes that the term is rather inapt. In a review of 4,000 consecutive patients that have come to his office, he found the incidence of migraine to be 22 per cent, of which 26 per cent occurred in women and 16 per cent in men. Goodman and Gilman point out that ergotamine tartrate (a drug used in the therapy of migraine) may, in some instances, produce precordial distress, but to our knowledge this has not occurred during therapy of migraine patients and was not found in our series.

Results

In our series of 684 patients suffering from migraine, 159 had some distress that suggested the presence of precordial types of migraine. The ages of the group and their distribution by decades may be seen in Chart I. By definition, all of these patients had cephalgia, so that the entire group had some type of headache associated with their symptoms. In this group also, there were vestibular disturbances in 132, ophthalmic disturbances in 135, and gastrointestinal disturbances in 148 of the patients (see Chart II). Of this entire group, palpitation was a predominant complaint in 83 (see Chart III). Usually, this occurred in conjunction with

CHART I

Age Distribution of Migraine Patients who had Precordial Symptoms	0-9	10-19	20-29	30-39	40-49	50-59	60-69	70-79
Male	0	0	5	12	7	10	6	1
Female	0	1	12	25	20	35	19	6
TOTAL	0	1	17	37	27	45	25	7

Males — 41
Females — 118
TOTAL — 159

CHART II

Other Systems Involved in Addition to Cardiac

Headache	159
Vestibular	132
Ophthalmic	135
Gastro-Intestinal	148

the attack of migraine, but may precede it, follow it, or it may occur without the headache, but with other signs suggesting a migrainous attack. Simple tachycardia occurred in 14, and paroxysmal tachycardia in three. These represented either seizures concomitant with cephalgia or they occurred in the absence of the headache but with other signs suggesting that they represented a migraine substitute. Pain in the chest nondescript in type was present in 92, and pain suggesting a rather definite anginal distribution was found in 37 of these patients. In the group of 158, there were 24 abnormal electro cardiograms (see Chart IV). In the rest, the electrocardiograms were normal. Hypertension was present in 43, and a Minnesota Multiphasic Personality Inventory applied to 34, revealed an abnormal test in 31. It was interesting to note that any combination of the so-called cardiac factors could be present during the seizure of cephalgia. The patient might have palpitation, tachycardia, chest pain, or anginal pain along with the headache, or these could follow the headache, occur singly or in any combination, and might occur in the absence of cephalgia. There was no correlation between the abnormal electrocardiogram or the hypertension with those patients who had the precordial type of migraine.

SUMMARY

In summary, 158 patients with migraine complained of signs and symptoms that were related to the thorax, suggesting that these patients may have precordial migraine. Palpitation occurred in 83, simple tachycardia in 14, and paroxysmal tachycardia in three. Nondescript types of chest pain occurred in 92 and a rather def-

CHART III

Cardiac Symptoms

Palpitation		83
Tachycardia	Simple	14
	Paroxysmal	3
Chest Pain		92
Anginal Pain		37

CHART IV

Other Cardiac Abnormalities

Abnormal ECG	24
Hypertension	43
M M P I Abnormal	31

inite type of anginal pain occurred in 37. These symptoms could occur not only with but also in the absence of the cephalgia, but because of associated and concomitant disturbances in other systems they were likely the result of migraine even when the cephalgic phase was absent.

CONCLUSIONS

When the precordial distress occurs in conjunction with an attack of cephalgia, the true nature of the chest distress is usually recognized. However, when the precordial pain or distress occurs as a migraine equivalent, failure to recognize it as such often leads to the erroneous diagnosis of organic heart disease. The establishment of the correct diagnosis in patients with precordial types of migraine when it is acting as a substitution or equivalent can only be made by obtaining a history that the seizures have occurred with cephalgia or have been part of a cephalgic phase or that they accompany other organic disturbances that have been characteristic in the individual of a migrainous seizure.

RESUMEN

En resumen, 158 enfermos con jaqueca se quejaron de signos y síntomas en relación con el tórax, lo que sugirió que estos enfermos podrían tener jaqueca precordial. Ocurrieron palpitaciones en 83, taquicardia simple en 14, y taquicardia paroxística en tres. Formas no descritas de dolor en el pecho se observaron en 92 y un tipo más bien definido de dolor anginoso se vió en 37. Estos síntomas podían ocurrir no sólo con la cefalalgia sino en ausencia de ella, pero a causa de los trastornos asociados y concomitantes en otros sistemas, es posible que fueran resultado de jaqueca aun en ausencia de la cefalalgia.

CONCLUSIONES

Cuando hay malestar precordial al mismo tiempo que una cefalalgia, la naturaleza del trastorno del torax es habitualmente reconocida. Sin embargo, cuando el dolor precordial o molestia, ocurre como equivalente de la jaqueca la falta de reconocimiento de la jaqueca en esa forma conduce al diagnóstico erróneo de un enfermedad orgánica del corazón. El establecimiento del diagnóstico correcto en enfermos con formas precordiales de jaqueca cuando es un substituto o equivalente, puede ser hecho cuando consta en la historia que los ataques han ocurrido con cefalalgia o han sido parte de una fase de cefalalgia o se acompañan de otros trastornos orgánicos que han sido característicos del ataque individual de jaqueca.

RESUME

158 malades atteints de migraines, se sont plaints de symptômes thoraciques qui pouvaient faire penser qu'ils étaient atteints d'un équivalent précordial de la migraine, 83 d'entre eux étaient atteints de palpitations, 14 de simple tachycardie, et trois de tachycardie paroxystique. Chez 92 malades, on constata l'existence de douleurs thoraciques sans caractère particulier, et chez 37 un tableau relativement précis d'angine de poitrine. Ces symptômes ont été constatés aussi bien en même temps que la céphalée qu'en son absence. On pouvait méanmoins en conclure, même en l'absence de céphalée, qu'ils étaient le résultat de la migraine, sur la constatation des autres manifestations viscérales associées et concomitantes.

En conclusion, quand les manifestations pré-cordiales surviennent en même temps que l'attaque des douleurs craniennes, on reconnait habituellement la véritable nature des troubles thoraciques. Cependant, la douleur précordiale ou les autres atteintes de cette région peuvent survenir comme un équivalent de migraine. Dans ce cas, lorsqu'on ne les reconnait pas, on peut les attribuer par erreur à une attaque organique du coeur. On peut établir correctement le diagnostic chez les malades lorsqu'il s'agit de manifestations d'un équivalent. Dans ce cas, on ne peut l'affirmer que par l'histoire qui révèle que l'attaque s'est accompagnée d'une migraine encéphalique, ou qu'elle accompagne d'autres manifestations organiques caractéristiques de l'attaque migraineuse chez ces malades.

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Primary Carcinoma of the Lung*

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Primary carcinoma of the lung, once considered a rarity, is now receiving repeated and intensive consideration in the literature. The question raised by many authors whether its apparent increase in incidence is relative or absolute cannot yet be answered with finality, but the general concensus appears to favor the former view. Increased longevity of the population, pre-employment chest x-ray films and other mass chest x-ray surveys, more refined diagnostic methods, and a clearer understanding of the origin of pulmonary neoplasia are factors which may account for its apparently higher incidence. Notoriously pleomorphic, many small cell anaplastic variants of primary lung carcinoma, such as the "oat cell carcinoma" of the English writers, were formerly classified as sarcomata, but now their bronchiogenic origin is definitely established.

Incidence: Primary lung carcinoma which now accounts for 5 to 20 per cent of all carcinomata, is of the same order of frequency as carcinoma of the large bowel, and is second only to carcinoma of the stomach as a cause of cancer death.[1] Like all cancers it may occur at any age, but surprisingly few cases are reported below the age of 40 years. In Bjork's series of 345 cases, 87.8 per cent were encountered in the fifth decade and over, the average being 55.4 years.[2] The right lung is more frequently involved than the left, and the upper lobes more commonly than the lower lobes.[4] Anywhere from 75 to 90 per cent of cases in any reported series are found in males, and the white to Negro incidence is given as approximately 2 to 1.[3] However, statistical analysis of the records of Harlem Hospital for the past five years tends to refute this axiom, and to indicate, instead, that when all other factors are equalized, the white to Negro incidence is nearly identical.

Etiology: The etiology of primary carcinoma of the lung will perhaps remain unsettled as long as the cause of malignant neo-

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plasia in general is unknown. Pneumoconiosis, especially silicosis, bronchiectasis, repeated pneumonitides, and increased population exposures to tarry road emanation have been at some time or other incriminated, but none of these factors are more than merely suspicious. Macklin[5] presents convincing evidence that no chronic inflammatory disease has been proved to be the cause of lung cancer, and that there is no significant difference in incidence in the presence of such diseases when corrected for age, sex, and other factors. Although they draw no conclusions Machle and Gregorius[6] observe a high incidence in workers of the chromate industry, and further indicate that of all chromate compounds the monochromates are the most carcinogenic. Boyd[7] points out that in the vicinity of Joachimstahl, Bohemia, where the basic industry is pitchblende (radium) mining, 90 per cent of all malignant tumors of the population occur in the lungs. In near-by Schneeberg, Saxony, there is a similar high incidence of primary lung cancer among cobalt miners. With the exception of asbestosis,[8] the pneumoconioses are now rather completely absolved as predisposing conditions. Tobacco smoking, the most commonplace source of potentially carcinogenic tar inhalation, is being scathingly examined as a possible etiologic factor, but no definite conclusions are yet admissable. However, Wynder and Graham[17] in an exhaustive analysis produce evidence that excessive and prolonged use of tobacco, especially cigarettes, seems to be an important factor in the induction of bronchiogenic carcinoma. It has been suggested, nevertheless, that the individual irritant itself may not be as significant as the chronicity of the patient's exposure to that irritant.[33]

Pathology: It is now known that with rare and questionable exceptions nearly all primary lung carcinomata arise from undifferentiated stem cells in the basal membrane of bronchi; therefore the term "bronchiogenic carcinoma" is a proper and accepted synonym for primary carcinoma of the lung. In over 90 per cent of cases these tumors are hilar in location, arising from a main stem bronchus or a secondary lobar bronchus; peripherally placed tumors are comparatively infrequent. In very rare instances the neoplasm may appear to arise from the alveoli, but Boyd[7] suggests that this falacious appearance often results from a surface spread of the tumor cells which may invade and line the alveoli in a manner suggesting the latter as the tissue of their origin.

The microscopic classification of primary lung carcinoma begs greater standardization, though certain difficulties are inherent in categorizing so pleomorphic a tumor. There are, first of all, various undifferentiated round, spindle, and "oat-cell" types formerly considered sarcomata. An epidermoid or squamous cell variety

is distinctly recognized, as is a glandular adenocarcinomatous type. Some authors speak of a "transitional" type as a more primitive variant of squamous cell carcinoma. The best working classification, therefore, appears to be (1) squamous cell or epidermoid (45-55 per cent); (2) small cell, anaplastic, and undifferentiated (25-40 per cent); and (3) adenocarcinoma (10-20 per cent). Of all three the squamous cell variety grows the most slowly and metastasizes latest. Since it remains confined to the hilum for a longer period of time it bears the best prognosis. The undifferentiated types and the adenocarcinomata run a more rapid course and metastasize early through the lymphatics and via the blood stream. The undifferentiated carcinomata are more likely to occur at an earlier age, and adenocarcinomas enjoy a high incidence in females.

Primary lung carcinoma is noted for its widespread metastases.[9] Its spread is threefold: locally through the lung; to lymph nodes; and to distant organs. However, the original growth may remain comparatively small while lymph node enlargement and even more distant metastases are considerable. The regional peribronchial and hilar lymph nodes, regardless of gross appearance, are considered involved in 100 per cent of cases which come to surgery, and their complete resection is always unqualifiedly attempted. The tracheal, supraclavicular, cervical, and axillary node chains are subsequently invaded in approximately that order. More than regional node involvement renders a case inoperable, as does, of course, more distant metastasis. The order of frequency of metastasis to distant organs is approximately: liver (50 per cent), pleura, adrenals, bone (especially ribs and spine), brain, kidney, and pericardium. Metastasis to the opposite lung is comparatively rare.

Diagnosis: The literature is replete with pleas for the earlier recognition of bronchiogenic carcinoma. This warning should be carefully heeded, for, as Overholt[10] suggests, this tumor is a common cause of cancer deaths, it is curable in the early stages, methods are available for the detection of early cases, and the majority of patients consult their physicians when the lesion is still operable. When the latter-most point is viewed against the light of Feld's and O'Malley's series,[11] in which there was an average physician delay of 4.3 months added to an average patient delay of 6.4 months, and the duration of life from the onset of symptoms to death 14.5 months, one can only join the chorus in urging that this menace be dealt with more promptly by the attending physician.

It might appear a platitude to state that the initial symptoms of primary lung carcinoma are referable to the respiratory tract, but so many of these insidious symptoms are dismissed by patient

and physician alike as "smoker's bronchitis," "middle age," and the like that this point bears underscoring. Localizing physical signs may be entirely absent in the early stages. More advanced cases are confounded with pulmonary tuberculosis, or are overshadowed by secondary complications such as atelectasis, lung abscess, and pleural effusions. On the other hand the presenting symptoms may already be those of metastases. With overshadowing extra-pulmonary manifestations the value of a correct diagnosis is more academic; it is the early case still amenable to surgical cure which must be detected promptly and treated with dispatch.

Although pulmonary tuberculosis and primary lung carcinoma may coexist, the usual danger is that of considering an incompletely studied case with moderate pulmonary findings as tuberculosis.[12,13] Indeed, where the two conditions co-exist it is thought more than likely in many cases that the carcinoma preceded the tuberculosis, debilitating the lung and rendering it an easy prey to invasion by the tubercle bacillus.[14] The presence of non-pathogenic acid-fast organisms in the sputum or gastric washings, combined with a possible if temporary weight gain on a sanitorial regime, may lead one completely astray. However, since the only hope for cure in primary lung carcinoma is early surgery, the temporization inherent in the usual management of pulmonary tuberculosis proves lethal. Feld and O'Malley[11] urge tuberculin testing as a routine, indicating that at least in some cases this error may be avoided by such a procedure.

The four most common early symptoms of primary lung carcinoma are cough, chest pain, dyspnoea, and expectoration, with or without hemoptysis.[15] This tetrad is due to bronchial irritation, obstruction, and/or ulceration. Chest pain is due to pleural and/or mediastinal involvement. In superior sulcus tumors invading the brachial plexus, pain in the corresponding arm may be the presenting symptom. On the other hand centrally placed tumors may cause mediastinal obstruction and impaired venous return, resulting in venous distension and cyanosis of the face, neck, and upper extremities.

Since over 90 per cent of these tumors are centrally placed, they may completely escape detection on physical examination early in their course. An obstructive wheeze, however, may be present, and contrary to popular belief, clubbing of the fingers may occur.[11] Weight loss, though also a constant finding, develops later. Therefore when any of the above symptoms occur singly or in any combination in an individual, especially male, over 40 years of age, primary bronchiogenic carcinoma must be ruled out regardless of physical findings. Since the detection of the

growth depends on the size and location of the mass, numerous diagnostic procedures may have to be followed before the true nature of the lesion becomes apparent.

Of the various laboratory tests an elevated erythrocyte sedimentation rate is the most constant finding. Hochberg[16] states that a highly characteristic blood picture in primary lung carcinoma is relatively normal or somewhat reduced hemoglobin, and leukocytosis with neutrophilia, especially in afebrile patients. Curious leukemoid reactions have been described by Henkin and others,[18-20] and probably represent bone invasion by tumor tissue. However, none of these findings are sufficiently specific to be more than corroborative evidence in the presence of more positive findings in the bronchial tree itself.

In early cases routine chest roentgenograms may be as fruitless as the physical examination, and should not awaken a false sense of security. In the comparatively infrequent peripheral tumor the nodule may be readily apparent, but since the usual location is central, the most characteristic finding is a perihilar mass, or mediastinal widening. If bronchial obstruction is sufficiently great, there may be secondary atelectasis, pneumonitis, and compensatory emphysema. In all questionable and/or suspected cases bronchoscopy is of paramount importance and will often yield information on the precise location of the tumor, extent of invasion and condition of the carina and trachea. It is also a means of securing a biopsy specimen if a growth is seen, or of obtaining bronchial secretions for cytologic study if no growth is evident in the range of bronchoscopic accessibility. However, upper lobe lesions defy thorough bronchoscopic evaluation because of technical difficulties, and peripheral lesions are beyond bronchoscopic reach. In these cases bronchography with radiopaque oil is a valuable ancillary procedure. Esophagrams may also be helpful, as may body section roentgenography.[21]

Of great promise in the early detection of primary lung carcinoma is cytologic examination of cellular detritus in the sputum and/or bronchial washings of suspected cases. Widely heralded and described independently by numerous authors whose methods differ only in technical details,[22-27] this procedure is valuable in accelerating the diagnosis in incipient or hidden cases. In expert hands its overall accuracy is placed at 80 to 90 per cent. Because of its relative technical simplicity, it might find application as a screening device in suspected cases, but it must not be supposed a diagnostic panacea, and every case must be judged in the light of all the available findings.

As a final diagnostic measure in cases of a static or progressive pulmonary lesion of unknown etiology where all other findings

TABULATED SUMMARY OF PROVED CASES OF BRONCHIOGENIC CARCINOMA SEEN ON THE CHRONIC CHEST SERVICE OF HARLEM HOSPITAL, NEW YORK CITY, 1945 - 1949 INCLUSIVE

Name	Age	Sex	Race	Duration of Symptoms Before Admission	Duration of Life After Admission	Primary Location of Tumor	Type of Tumor
L.R.	44	M	N	1 month	91 days	Left main bronchus	Squamous cell
E.F.	58	M	N	4 months	91 days	Left main bronchus	Anaplastic
J.L.	66	M	N	3 weeks	—	Right main bronchus	?
I.S.	67	M	N	2 months	—	Right stem bronchus	Anaplastic
S.D.	66	M	N	6 months	—	Left main bronchus	Squamous cell
J.F.	35	M	N	3 months	23 days	Right lung	Anaplastic
M.P.	47	F	N	6 months	—	Right main bronchus	Anaplastic
A.B.	46	M	N	5 weeks	—	Right lung	Squamous cell
A.H.	39	F	N	3 weeks	49 days	Right main bronchus	Anaplastic
J.H.	66	M	N	2 years	10 days	Left lung	?
J.J.	63	M	W	6 months	17 days	Left lung	Squamous cell
M.C.	75	F	N	2 days	38 days	L.U.L. bronchus	Anaplastic
J.W.	39	M	N	6 months	30 days	Right lung	Squamous cell
J.B.	44	M	N	2 months	59 days	Right main bronchus	Anaplastic
H.B.	59	M	N	6 months	56 days	R.L.L. bronchus	Squamous cell
J.M.	41	M	PR	4 months	50 days	R.L.L. bronchus	?
F.S.	63	M	N	14 weeks	—	R.U.L. bronchus	Squamous cell

TABULATED SUMMARY (Continued)

Name	Age	Sex	Race	Duration of Symptoms Before Admission	Duration of Life After Admission	Primary Location of Tumor	Type of Tumor
J.S.	61	M	N	3 months	—	R.U.L. bronchus	Squamous cell
C.J.	44	M	N	1 year	22 days	Right main bronchus	Squamous cell
J.M.	46	M	N	3 weeks	80 days	Right main bronchus	Squamous cell
P.Y.	41	M	N	5 months	46 days	L.U.L. bronchus	?
S.S.	59	M	N	1 month	64 days	R.L.L. bronchus	Adenocarcinoma
G.C.	63	F	N	several months	7 days	R.U.L. bronchus	Anaplastic
J.D'S	44	M	W	7 months	35 hays	Right lung	Adenocarcinoma
W.L.	56	M	N	3 months	43 days	Left main bronrhus	Anaplastic
P.J.J.	43	M	N	7 months	44 days	R.L.L. bronchus	Squamous cell
L.T.	44	M	N	few days	—	Right main bronchus	?
W.B.	33	M	N	3 weeks	62 days	Right lung	Anaplastic
TOTALS:		24M 4F	25N 2W 1PR			Left lung 8 Right lung 20	Squamous cell 11 Anaplastic 10 Adenocarcinoma 2 Undetermined 5
Averages	51.8 years			18.5 weeks	46.5 days		

are negative exploratory thoracotomy is an urgent necessity. But needle biopsy is universally condemned as a dangerous and inexcusable undertaking.[11]

Complications: The two most common intrathoracic complications of primary lung carcinoma are pleural effusion and lung abscess. Pleural effusion need not necessarily be present in all cases, and if so, it is not always sanguinous. The differential cell count of pleural effusion is of no practical significance, but the presence of definite tumor cells indicates metastasis to the pleura, a stage beyond the hope of surgical cure.

More treacherous in masking the presence of a primary neoplasm is an associated lung abscess. There are several ways by which localized suppuration may evolve in the presence of an obstructive lesion. The growth may become infected, and form an abscess per se. It may produce obstruction of a bronchus, causing atelectasis and suppurative pneumonitis in the distal lung segment. There may be spillage of infectious material into healthy pulmonary tissue, setting up multiple abscesses. Finally, there may be any combination of these routes. Regardless of the mode of origin, the suppuration may dominate the scene, and the underlying nature of the lesion remain obscure. In Brock's series of 405 cases of lung abscess, bronchiogenic carcinoma was the etiologic factor in 13.8 per cent of all cases, and in 30 per cent of cases 45 years of age and over.[28] Brock admonishes that multiple or bilateral abscesses in an individual 45 years of age or over should focus attention on the true possible cause of the disease. Complications arising from distant metastases are useless signs from the standpoint of effecting a cure.

Treatment: The only hope for cure in primary lung carcinoma is total pneumonectomy with complete resection of the bronchial and mediastinal nodes. Any measure short of this will inevitably lead to failure. Age alone is no contraindication to surgery, nor are small fluid collections present in conjunction with atelectasis. Definite contraindications are: (1) tracheal or carinal involvement; (2) pleural effusion with tumor cells; (3) paralysis of the diaphragm and/or vocal cords; (4) definite evidence of distant metastasis; and (5) poor general condition. The operative mortality varies in the literature from 20 per cent to less than 4 per cent,[29] and the resectability at operation from one out of three to one out of five cases.[3,30] There is a five year survival rate in about 8 per cent of the cases.

Mustard gas has been used, but, like radiotherapy, is only palliative, and the best response is obtained with the more undifferentiated cellular type.[31] However, in all inoperable cases radiotherapy is the treatment of choice. Widman[32] claims that

radiotherapy will prolong life one year or longer in 10 per cent of all patients regardless of the cellular character of the lesion.

Case Studies: During the five year period 1945-49 inclusive, 88 cases of primary carcinoma of the lung have been seen on the Chronic Chest Service of Harlem Hospital, New York City. Since Harlem Hospital is located in a predominantly Negro community, the numerical modesty of this series is due largely to the fact that as in other underprivileged areas, pulmonary tuberculosis tends to make the heaviest demands on available hospital chest facilities. However, of the total number of cases of bronchiogenic carcinoma 75 cases or 87.5 per cent of the total number were Negro, seven or 11.4 per cent white, and three or 1.1 per cent Puerto Rican. These percentages roughly parallel the total number of admissions to Harlem Hospital by percentage of the three races mentioned. From this series, therefore, the conclusion is tenable that in a predominantly Negro community the white to Negro incidence is unity. It appears more than likely that the commonly entertained impression of a greater incidence in whites (usually given as 2 to 1) has resulted merely from an inadequate number of Negro admissions to the hospitals where the classical data have been compiled. In any event, further studies are strongly indicated.

Although this series has been collected on the basis of clinical, radiologic, and/or bronchoscopic evidence, 28 cases of the total, or 31.8 per cent have been confirmed histologically by biopsy or autopsy. The remaining 60 cases died without post-mortem examination or left the hospital against advice and disappeared from follow-up before the diagnosis could be proved histologically.

Of our 28 proved cases 14 were confirmed by bronchoscopic biopsy, five by autopsy, four by specimens obtained at exploratory thoracotomy, three by lymph node biopsy, one by aspiration biopsy of the lung, and one by Pappanicoloau smear of bronchial secretions. Twenty-four (86 per cent) are males and four (14 per cent) females. The age range is from 33 to 75 years, with an average of 51.8 years. The duration of symptoms prior to admission is from a few days to two years, with an average of 18.2 weeks, and the duration of life after hospital admission is from seven to 91 days, with an average of 46.5 days. Although in some cases symptoms undoubtedly lasted longer than the period stated by the patient, nevertheless an inverse relationship tends to exist between the duration of symptoms prior to admissions and the duration of life after admission. The primary location of the tumor is left main bronchus in four cases, left upper lobe bronchus in two, left lung, bronchus undetermined in two, right main bronchus in eight, right upper lobe bronchus in four, and right lung, bronchus undetermined, in five cases. Thus, the location of the tumor is in

the left lung in eight (28.6 per cent), and in the right lung in 20 (71.4 per cent). The tumor type is epidermoid in 11 (38.5 per cent), anaplastic in 10 (35 per cent), and adenocarcinoma in two (7 per cent). The tumor type is unspecified in 5 (17.5 per cent).

SUMMARY

The incidence, etiology, pathology, diagnosis, complications, and treatment of primary carcinoma of the lung are discussed in the light of the most recent beliefs. A statistical analysis of cases seen on the Chronic Chest Service of Harlem Hospital, New York City, during the five year period 1945-49 inclusive, is given, and summaries of 28 histologically proved cases are presented. It is significant that of these 28 proved cases the average age is 51.8 years. There is a ratio of six males to one female. The average duration of symptoms before seeking medical care is about four months; the average longevity after hospitalization, one and one-half months. The primary lesion was in the right lung more than twice as often as in the left. Over 70 per cent were represented almost equally by the anaplastic and squamous cell types, while about 17 per cent were unclassified and 7 per cent were adenocarcinomas.

Also apparent is the fact that none of the cases were seen early enough to be benefited by any known form of therapy, far less to be cured.

Knowledge of the subject of bronchiogenic carcinoma to date indicates that the best chance for the cure of this disease lies in its early discovery, preferably before there are noticeable symptoms on the part of the patient. Thus, yearly chest x-ray film inspection of all persons and routine chest x-ray films of all hospital admissions should be common medical practice.

Further, there should be less procrastination on the part of patients, physicians and surgeons to proceed with surgical exploration whenever a suspicious lesion presents itself in which the bronchoscopic and cytological studies are inconclusive or negative because of inaccessability, encapsulation or failure to extend to the surface mucosa. Especially, since it is known that between 25 and 30 per cent of the cases fall in this group when first discovered.

It is noteworthy that the incidence percentage of white to Negro in this series roughly parallels the admission percentage to Harlem Hospital of these respective races. The belief is expressed that no apparent racial predilection would be found to exist in primary carcinoma of the lung if sufficiently large segments of the Negro population were studied.

RESUMEN

Se discuten a la luz de los conocimientos actuales la incidencia, la etiología, la patogenia, el diagnóstico, las complicaciones y el tratamiento del carcinoma primario del pulmón.

Se presenta un análisis estadístico de los casos vistos en el Servicio de Torax del Hospital de Harlem de New York City durante cinco años de 1945 a 1949 inclusive y se relatan resúmenes de 28 casos comprobados histológicamente.

Es de llamar la atención que en estos 28 casos la media de la edad sea de 51.8 años.

Hay una proporción de seis varones por una hembra.

El término medio de duración de los síntomas antes de que se recurriera a atención médica es de cuatro meses. La media de longevidad después de la hospitalización es de uno y un mes y medio. La lesión primitiva estuvo ubicada en el pulmón derecho mas de dos veces mas a menudo que en el izquierdo. Mas del 70 por ciento estaba representado por tumores anaplásticos y de celdillas escamosas mientras 17 por ciento eran de no clasificados y 7 por ciento de adenocarcinomas.

Es también aparente el hecho de que ninguno de los casos fué visto con suficiente precocidad para ser beneficados por forma alguna de tratamiento y mucho menos para ser curados.

El conocimiento del carcinoma hasta ahora indica que las mayores probabilidades de curación dependen de su descubrimiento temprano, de preferencia cuando aún no hay síntomas percibidos por el enfermo. Por tanto la inspección por medio de radiografías anuales de todas las personas y la radiografía de rutina en todo caso que ingresa al hospital debe ser una práctica común en medicina.

Además debe haber menos tendencia a demorar la exploración quirúrgica cuando una lesión sospechosa se presenta cuando la broncoscopía y el exámen citológico no sean concluyentes o sean negativos ya sea por la inaccesibilidad, por la encapasulación y porque no haya invasión de la mucosa.

Esto debe tenerse en cuenta en particular puesto que del 25 al 30 por ciento de los casos están en estas circunstancias cuando se descubren.

Es digno de notarse que el porcentaje de incidencia en las razas negra y blanca es sensiblemente paralelo cuando se admitieron en el Hospital de Harlem. Se expresa la creencia de que no hay aparente predilección por la raza negra para el carcinoma primitivo del pulmón si se estudian números importantes de individuos en la población.

RESUME

L'auteur étudie la fréquence, l'étiologie, l'anatomie pathologique, le diagnostic, les complications et le traitement du cancer primitif du poumon à la lumière des conceptions les plus récentes.

Il donne une analyse statistique des cas qui ont été constatés pendant une période de cinq ans (1945-49) dans le service d'affections pulmonaires choniques de l'Hôpital de Harlem (New York City). Il présente les résumés de 28 cas histologiquement démontrés. Sur les 28 cas, l'âge moyen est de 51.8 ans. On compte six individus du sexe masculin pour un du sexe féminin. Le temps moyen qui sépare l'apparition des symptômes de la prise en charge par le médecin est d'environ quatre mois. La survie moyenne après hospitalisation est de un mois à un mois et demi. La lésion primitive se trouve deux fois plus souvent dans le poumon droit que dans le gauche. Presque 70% des cas étaient représentés par des formes épidermoïdes, alors que 17% des cas ne pouvaient être classés; et que dans 7%, il s'agis sait d'adéno-carcinomes.

Il apparait clairement qu'on ne vit aucun de ces cas suffisamment tôt pour le faire bénéficier des thérapeutiques actuellement connues, et encore bien moins pour en espérer la guérison.

Ce que l'on sait actuellement du cancer bronchogénique indique que la meilleure chance de traitement de l'affection dépend de sa découverte précoce, de préférence avant que le malade ait remarqué aucun symptôme. C'est dire que l'examen radiologique annuel du thorax chez tous les individus et l'examen systématique par radiographie de tout malade admis dans un hôpital devrait être de pratique courante.

De plus, il devrait y avoir moins d'hésitation de la part des malades, des médecins, et des chirurgiens, à pratiquer une exploration chirurgicale chaque fois qu'une lésion semble suspecte, même quand la bronchoscopie et l'examen cytologique ne sont pas concluants ou sont négatifs. C'est l'impossibilité d'atteindre la lésion, son encapsulation ou son absence d'extension à la surface de la muqueuse qui sont responsables de ces résultats. Nous savons maintenant que 25 à 30% des cas découverts pour la première fois appartiennent à cette catégorie.

Le pourcentage du cancer primitif du poumon chez les blancs ou chez les nègres est exactement parallèle au pourcentage d'admissions à l'hôpital de Harlem de ces deux catégories d'individus. L'auteur émet l'opinion qu'on ne trouverait aucune prédisposition ethnique si on envisageait l'étude d'une partie suffisamment importante de la population noire.

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Alveolar Cell Tumor of the Lung

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Of the primary tumors of the lungs, the alveolar cell type is believed to be rare.[1] Our case is of interest because of its rarity, duration and autopsy findings. The historical data and other pertinent facts, including etiology, signs, symptoms and pathology have been discussed in detail by Ikedea.[1] According to Ewing the tumor occurs in two forms;[2] the nodular and the more diffuse or pneumonic type. The lesions may be restricted to one or more lobes and they may be unilateral or bilateral. The bronchi are not involved except as result of invasion by the nodular areas. Metastases do take place to regional lymph nodes and on occasion to distant organs. Clinically the symptoms are most often atypical and misleading. Death in the reported cases is usually secondary to widespread involvement of the lungs creating asphyxia and rarely due to extensive visceral or cerebral metastases.

The first case of diffuse alveolar cell carcinoma, of the type we are reporting, was described in 1903 by Musser.[3] This was a 47 year old man whose chief complaint was soreness of throat at night, expectoration of mucoid material in large quantities, progressive dyspnea and cough. His death occurred three weeks after a diagnosis of tuberculous bronchopneumonia was made and the autopsy revealed the typical picture of primary carcinoma of the lung, originating in the alveolar epithelium. The only metastases found at the time of autopsy were in the regional lymph nodes.

The symptoms, which have been enumerated by some authors,[4-6] are variable and usually those ascribed to carcinoma of the lung of bronchogenic origin. These are cough, presence of bloody sputum, pain in the chest, cyanosis, pleural effusion and loss of weight. In other cases fever, non-productive cough, prostration and other constitutional symptoms of an inflammatory lesion predominate. In the presence of diffuse involvement pneumonia is often suspected. Bronchoscopic examination usually furnishes no diagnostic information. The roentgenograms show a variable picture, depending upon the type of alveolar cell tumor present. In the nodular or miliary type there may be punctate infiltrations resembling the mottling of miliary tuberculosis or metastatic

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carcinoma. In the diffuse or pneumonic type the picture of lobar pneumonia is often simulated. The middle lobe syndrome[7] or chronic atelectasis and pneumonitis[8] may be confusing in the differential diagnosis of this condition. Treatment recommended for alveolar carcinoma of the lung is excisional surgery when possible and radiation therapy as an adjunct in palliation of the advanced case. The majority of reported cases have died within a year.

Case History

I.G.P., a 34 year old white male, first consulted one of us (J.N.W.) in March 1946, at which time he complained of a sudden onset of coughing of six days duration and which was productive of sputum streaked with blood. In addition there was an associated severe pain in the right lower chest, which resembled pleurisy. The past history dated to 1939 when he was first seen and treated in Longview, Texas; at that time a diagnosis of unresolved pneumonia of the right lower lobe was made (Figure 1). He continued to have intermittent attacks of cough, chest colds and fever until July 1941, when he was in an automobile accident and sustained an injury to the right side of his chest. There were no fractures at that time, however, x-ray films revealed a pneumonic type process in the lower portion of the right lung field. In January 1942 he was again hospitalized for an exacerbation of his pulmonary symptoms and the pathology which had been previously described in the right lower chest was still present but had become more extensive (Figure 2). The diagnosis of pneumonia, right lower lobe, type undetermined, was made. In December 1942, he was again hospitalized for the pulmonary condition, at which time symptoms and physical findings were essentially the same as before. He was treated with chemotherapy and oxygen and at the time of dismissal the diagnosis of unresolved pneumonia of the right lower lobe was again made. Sputum examinations were negative for tubercle bacilli, spirochetes or fungi. He was next hospitalized in December 1945 for an exacerbation of the pulmonary symptoms and again the diagnosis of pneumonia of the right

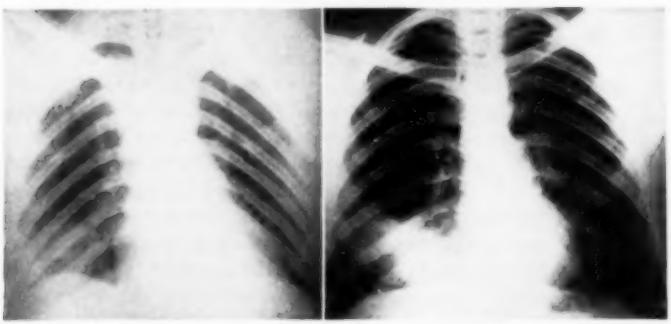

FIGURE 1 FIGURE 2

Figure 1: Original x-ray film taken December 1939, showing lesion in lower right lung field.—*Figure 2:* Same process increased in extent.

lower lobe was made. The disease, however, was more extensive in the right chest and at this time was first noted to involve the left lower lung field. His next admission was in March 1946, when he was first seen by one of us (J.N.W.). During the preceeding year he had lost approximately 35 to 40 pounds in weight. X-ray film inspection revealed evidence of consolidation in the lower portion of the chest on the right and a probable pneumonic process in the lower lobe of the left lung. The diagnosis of bilateral pneumonia was entertained. He was treated with antibiotics and discharged after the acute exacerbation of his pulmonary symptoms had subsided. During the period of hospitalization he was raising copious amounts of thick, frothy, mucopurulent blood tinged sputum. A daily record of this sputum was kept and ranged from 830 cc. to 1200 cc. daily. Examination of the sputum showed no acid-fast organisms, spirella, or fungi. There were numerous pus cells and the sputum had an offensive odor. No organisms were found on gram stain. He was bronchoscoped by (L.K.T.) on March 20, 1946 and moderate narrowing of the openings into the right lower and middle lobes with reddening of the mucosa of both bronchi was noted. No tumor masses could be seen. The bronchoscopic diagnosis of bronchial stenosis, right lower and middle lobes was made.

The patient was referred to one of us (G.F.M.) in April 1946, and after examination, including AP and PA and lateral films of the chest, as well as bronchoscopy, a tentative diagnosis of carcinoma or chronic pneumonitis and atelectasis was entertained with disease involving the right middle and lower lobes, as well as the left lower lobe. Because of the duration of the disease and the severity of the cough with hemoptysis and marked expectoration, it was felt that an exploration was indicated and this was accordingly carried out by one of us (G.F.M.). At the time of exploration the pathologic process was found chiefly in the right middle and lower lobes but also was present in the right upper lobe (Figures 3 and 4. The exact nature of the lesion was not determined. Frozen sec-

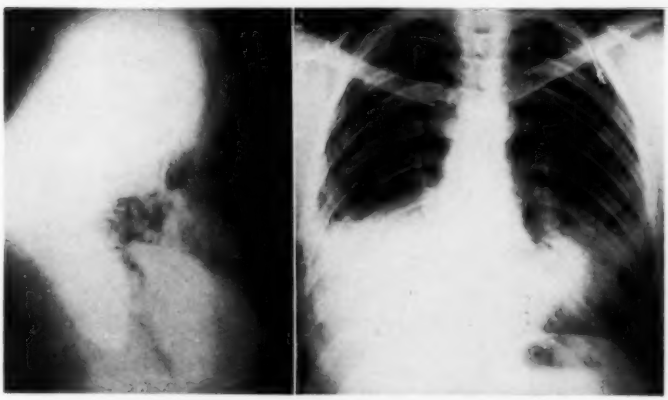

FIGURE 3 FIGURE 4

Figure 3 - 4: P.A. and lateral films showing evidence of disease in both lung fields with chief involvement in right middle lobe.
Figure 4: P.A. post-operative film.

tions were not obtained. Had we known that the underlying process was malignant any operative procedure carried out to effect a cure would have required a total right pneumonectomy, as well as a left lower lobectomy. This, however, would have been too extensive because of his already limited respiratory reserve. Because the chief pathology in the right chest involved the middle lobe, a right middle lobectomy was done and he did well post-operatively. He was seen as an out-patient in the summer and fall of 1946, when he gained rapidly in weight to a maximum of 152 pounds. The sputum was reduced from a maximum of 1200 cc. to an average of 150 cc. of clear, frothy sputum daily. His condition remained satisfactory for two and one-half years and he returned to work. In the latter part of 1948 he had a gradual decline in general condition. He had been given x-ray therapy post-operatively but had not returned for his full course of treatment. In March 1949 the patient developed some numbness and weakness of the left arm and left leg. The diagnosis of possible cerebral metastasis was made. X-ray film inspection showed the pulmonary process to have become more extensive. Bronchoscopic examination done elsewhere (University of Texas) showed nothing startling save the excessive amount of secretion which was mucopurulent. There was no tumor tissue seen which was possible to obtain by biopsy. The patient's weight had reduced to 129 pounds in June 1949. In the fall of 1949 he developed visual difficulties which developed almost to a point of total blindness and the numbness and pain in the left arm and left leg progressed. He was dyspneic and cyanotic most of the time. His condition was progressively downhill until January 1950, when he became delirious and died.

Surgical Specimen: Submitted by G.F.M. on April 20, 1946, consisted of the middle lobe of the right lung. No detailed record was made of the size, weight, or appearance of this lobe. Microscopic sections showed neo-

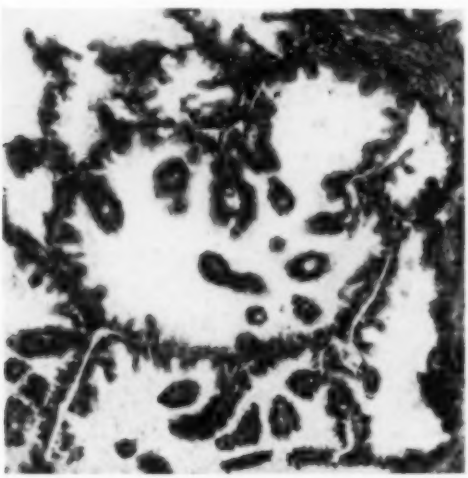

FIGURE 5: The surgical specimen showing the diffuse involvement of the lung alveoli. (x150).

plastic changes involving all of the alveoli. The pattern of the alveoli was moderately well preserved. The lining carcinoma cells were tall columnar, with nuclei placed near the base. No cilia were present. The nuclei stained densely and in areas showed pleomorphism. In some alveoli these neoplastic cells were present as a single layer, while, in others, they had proliferated to form both solid nests and papillary projections. The cells had produced a marked amount of mucin as demonstrated by Azure-A. This mucin was present in the form of globules in the cytoplasm of some neoplastic cells and also filled most of the alveolar spaces (Figure 5).

Autopsy: On January 16, 1950, this study revealed alveolar carcinoma involving the entire remaining right lung, the left lower lobe, and about one-half of the left upper lobe. Metastatic deposits of alveolar carcinoma were found in the right cerebral hemisphere, in two tracheobronchial nodes, in one preaortic node (celiac node), and in the liver. No additional pathology of importance was noted in the remainder of this post mortem examination except dense pleural adhesions. The right lung was so adherent to the chest cavity that it could not be removed as a complete organ. The left lung weighed 1000 grams. On the pleural surface numerous nodules were seen that appeared slightly elevated and grayish-yellow in color. On cut section this same nodular pattern was observed but the nodules were confluent. There was no evidence that the carcinoma had its origin from any of the bronchi. Glairy mucus could be scraped from the cut surface. The main bronchi also contained this type of secretion.

The tumors in the right cerebral hemisphere were about three centimeters in diameter and were found in the superior pre-frontal area and in the superior parietal lobule. The tumors were made up of mucus for the most part (Figure 6).

The metastatic deposits in the lymph node and in the liver were more solid in character (Figure 7).

The microscopic appearence was similar to that described in the surgical specimen. However, one interesting thing was noted in the lung concerning the distribution of the neoplastic tissue. There were areas

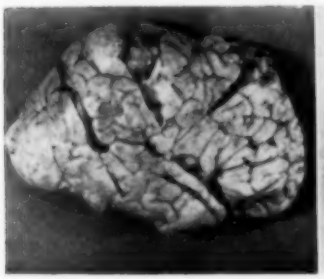

FIGURE 6

FIGURE 7

Figure 6: Right cerebral hemisphere, showing the two metastases. They are seen as projecting tumors over the convexity of the cerebral hemisphere. (Reduced to one-fifth actual size).—*Figure 7:* Liver, showing the two metastatic deposits, one subcapsular and the other slightly below the surface. (Reduced to one-fifth actual size).

where all of the alveoli were definitely involved by carcinoma, and then other areas where small, discrete nodules could still be detected. In the latter areas, occasionally, only one-half of an alveolus would show tumor tissue.

The intervening lung appeared normal, thus ruling out pulmonary adenomatosis. The amount of mucus produced was marked in the lung and in the brain. The metastases in the lymph nodes and in the liver showed both gland formation and solid strands of tumor cells.

The problem of differentiating pulmonary adenomatosis from alveolar cell carcinoma is real but the recent work by Laipply and Fisher[11] with their illustrations has helped define the two diseases. As they stressed, pulmonary adenomatosis shows " alveoli lined with epithelium-like cells, marked fibrosis, and lymphocytic infiltration of interalveolar septums, lining alveolar cells are columnar or cuboidal, are usually nonciliated, and are uniform in size, shape, and staining reaction. Mitotic figures are few and there is no invasion of adjacent tissue."

In contrast alveolar carcinoma, as demonstrated by this case, shows diffuse and nodular involvement of the lung, essentially normal intervening lung tissue when present, cellular plemorphism, and metastases. If these differences are kept in mind, the two diseases can be microscopically differentiated.

Final Diagnosis: Alveolar cell carcinoma of the lung with metastases to lymph nodes, liver and brain.

Discussion

The tumor in this patient was undoubtedly present for at least 11 years. Although the patient was seen throughout this period by a number of physicians, the most frequent diagnosis entertained was unresolved pneumonia. Congenital atelectasis with pneumonitis and carcinoma were considered at the time of his hospitalization in 1946. The chief symptom was productive cough and on some occasions it amounted to 1200 cc. of sputum daily. The patient was given considerable palliation by surgical excision of the right middle lobe and subsequent x-ray therapy. We feel that the tumor variety we are dealing with was that of a pneumonic type of alveolar cell carcinoma of the lung. The tissue has been studied by one of us (L.R.H.) and Dockerty,[10] both of whom concur in the diagnosis. This case is another example of how closely carcinoma of the lung can simulate both clinically and roentgenographically other pulmonary lesions. It also demonstrates the fallacy in adopting the policy of waiting, watching, and taking frequent roentgenograms. Had this lesion been more localized at the time of exploration, the possibility of a cure could have been entertained, however, the extensiveness of the lesion was such

that total extirpation of the entire pathology was impossible. We believe this to be the longest case on record in which the disease, which was first noted in the lung in 1939, persisted by roentgenographic evidence for a period of 11 years before death ensued. The patient had exacerbation of symptoms when an inflammatory process was superimposed on the existing lesion, however, the acute symptoms responded to antibiotics and oxygen therapy. He was never completely free of symptoms following his original illness in 1939. Successive x-ray films during the 11 year period showed extension of the process. This lesion should have been subjected to exploratory thoracotomy much earlier in its course. In addition, it demonstrates the slow growth of the neoplasm and the palliation which resulted from the removal of a portion of the involved lung followed by x-ray therapy. The case of Delarue and Graham[5] would seem to substantiate this contention. In addition, it is an example of alveolar cell carcinoma of the lung which metastasized widely.

SUMMARY

1) Alveolar cell tumors of the lung are rare and present symptoms which are often atypical and misleading.

2) This tumor occurs in two forms, i.e. nodular or miliary variety and a diffuse or pneumonic type.

3) A case is reported in whom an alveolar cell tumor existed for a period of 11 years before death occurred. Symptoms had been attributed to unresolved pneumonia throughout the major part of its course.

4) Excisional surgery, where possible, is the treatment of choice but roentgen therapy is of aid in the inoperable case.

5) Metastases usually occur only to regional lymph nodes. In the case presented, distant metastases were also found.

RESUMEN

1) Los tumores de celdillas alveolares del pulmón son raros y presentan síntomas que son a menudo atípicos y engañosos.

2) Estos tumores ocurren en dos formas: nodular o miliar y una forma difusa de tipo neumónico.

3) Se refiere un caso en el que el tumor alveolar existió por 11 años antes de descubrirse. Los síntomas se atribuyeron a neumonía no resuelta durante la mayoría del tiempo de su evolución.

4) La cirugía de excisión es el tratamiento de elección cuando es posible pero la roentgenterapia es útil en los casos inoperables.

5) Las metástasis ocurren generalmente solo en los ganaglios regionales. En el caso relatado también había metástasis a distancia.

RESUME

1) Les tumeurs du poumon d'origine alvéolaire sont rares et se présentent souvent sous un aspect symptomatique atypique et trompeur.

2) Ces tumeurs se présentent sous deux formes: la forme nodulaire ou miliaire, et la forme diffuse ou pneumonique.

3) Les auteurs rapportent une observation dans laquelle une tumeur à cellules alvéolaires évolua pendant onze ans avant l'apparition de la mort. Pendant la plus grande partié de l'évolution, des symptômes furent attribués à une pneumonie à résolution incomplète.

4) Le traitement de choix est l'exérèse chirurgicale quand elle est possible, mais dans les cas inopérables, le traitement radiothéapique est un auxiliaire précieux.

5) En énéral, les métastases se font dans les lymphatiques régionaux. Dans le cas rapporté, il y avait également des métastases à distance.

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Treatment of Spontaneous Pneumothorax by Means of Continuous Intrapleural Suction

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This report describes a method of obtaining constant negative intrapleural pressure and the results of its application in treatment of 10 patients with spontaneous pneumothorax. This condition is considered here as the onset of pneumothorax without known trauma, and without causative infectious pulmonary disease. Spontaneous pneumothorax is most common in the young and apparently healthy adults, most of whom give no history of previous pulmonary disease. It may occur at rest or during exercise. The initial or chief symptom is usually pain which is pleuritic in type. Depending upon the degree of collapse, and the severity of pain, there is a variable dyspnea which may be present only during exercise. Confirmation of the diagnosis depends upon x-ray studies demonstrating the pulmonary collapse. Generally the condition is benign, responding to simple rest with spontaneous expansion of the lung. The time for expansion ranges from days to weeks and in some cases the lung will not expand even after prolonged rest. Published series show the time for expansion from simple bed rest varying between two days to several months.[1-3] Studies have also shown recurrences in large groups of patients between five and 38 per cent.[2-5]

Spontaneous pneumothorax in apparently healthy young individuals is probably not associated with tuberculosis any more frequently than that which occurs in the general population. Pleural fluid collection does not imply tuberculosis. Ornstein and Lercher[3] noted small pleural effusions in 22 of their 58 patients with spon-

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taneous pneumothorax, none of whom had tuberculosis, and this finding is borne out by other authors.[5,6]

Probably the most common immediate cause of the pneumothorax is a rupture of a subpleural bulla or cyst. The majority of this type of predisposing cystlike structures arise in the apex. Hamman's clinical material and Macklin's experimental results[7,8] suggest a different causative mechanism; namely, that following rupture of an alveolar space, due to increased pulmonary pressure air enters the interstitial tissue and dissects along the pulmonary vessels where it enters the mediastinum. A sufficiently large amount of air may then enter the pleural space at the point of least resistance. In spite of scattered case reports of concurrent pneumo-mediastinum and pneumothorax, there is a paucity of clinical evidence to support this view. Most patients will not have evidence either by physical examination or x-ray film of pneumomediastinum with their pneumothorax and conversely a large number will have easily demonstrable blebs and cysts.

Among patients with spontaneous pneumothorax there will be a small number so acutely ill from diminished respiratory capacity as to require emergency treatment. These individuals will have tension pneumothorax, bilateral pneumothorax, hemopneumothorax, or simple pneumothorax superimposed on an already marginal pulmonary reserve. These patients obviously require an immediate decompression which is afforded by an intrapleural catheter connected to an underwater seal drainage. The majority of patients will not present such emergencies and will improve without special treatment. There are some aspects in the treatment of non-emergency spontaneous pneumothorax which forces more aggressive treatment than simple rest; these are, the economic loss resulting from the frequently prolonged bed rest necessary for expansion of the lung, and, secondly the possibility of recurrent pneumothoraces.

The practical management of a patient with non-emergency spontaneous pneumothorax involves an individual appraisal of each case. It must be determined whether serious underlying pulmonary disease exists. This is particularly important if obliteration of the pleural space as a subsequent prevention of future collapse is being considered. Careful history and physical examination on entry, together with routine laboratory studies and chest x-rays, supply the necessary information for intelligent appraisal of this point. If the patient has not had previous pneumothorax and is relatively asymptomatic, a short period of hospital observation may be tried. If his lung begins to expand after rest alone, it is reasonable to allow him up to two weeks to complete his reexpansion and much of this time may be spent at home.

A week of light activity following reexpansion should offer as much safety against recurrent collapse as a considerably longer time would. In the refractory or recurrent pneumothorax attempt should be made to expand the lungs quickly and permanently. Various substances introduced intrapleurally with the hope of causing sufficient adhesions between the pleurae to prevent further collapse have been tried. Usually this method has been attempted after prolonged bed rest with failure of expansion. Hennell and Steinberg,[9] Taschman[10] and Hetherington and Spencer[11] have reviewed the technics used in this procedure. They require a prolonged time and cause considerable discomfort to the patient. There is also the possibility of causing such a marked pleuritic reaction as to prevent expansion and necessitate a future decortication.

Surgical intervention with open thoracotomy has been tried on occasion. These procedures usually involve suturing the point of rupture or inverting the suspicious area of emphysematous lung. The involved area has also been removed by segmental resection or lobectomy.[12-15] It is the feeling of the authors that thoracotomy should be reserved for patients in whom open intervention is necessary because of serious hemothorax with pneumothorax or chronic pneumothorax with a cortical layer on the pleura that prevents expansion; or where the underlying disease is such that a cure can be expected only by resection and adequate pulmonary tissue can still be preserved. From studying the reviews of spontaneous pneumothorax, one may expect these cases to be in the minority.

An ideal treatment for recurrent or refractory pneumothorax should offer the patient a rapid return to work with a reasonable chance of permanent cure. The treatment should have a very low risk. Continuous intrapleural suction produces an immediate expansion. The objection that the pleural rent may be held open is invalid since suction pulls the air out faster than it can leak from the pleural rent. The lung is then pulled against the chest wall and within a short time the rent is effectively sealed. If a pleuritis develops because of continuous suction the pleural symphysis, which may occur, offers the same bar to further collapse as any symphysis caused by a pleural irritant. In none of our cases did any bacterial contamination of the pleural fluid occur. In most cases treated by this method it is possible for the patient to leave the hospital within a week's time. There are few references in the literature to the use of continuous intrapleural suction as a definitive method of therapy. Hawkins in 1948[16] treated a 31-year old male with recurrent bilateral pneumothorax and after unsuccessful attempts to symphysis by silver nitrate and glucose,

continuous intrapleural suction for 14 days was successful in expanding the left lung. The right lung was later expanded by a similar procedure. Smart in 1949[17] suggested that continuous intrapleural suction would be desirable in tension pneumothorax but gave no details.

Technic of Continuous Intrapleural Suction

After completion of the initial studies which have reasonably ruled out serious underlying pulmonary inflammatory disease or any condition where an obliterative procedure might be contraindicated, the patient is taken to surgery. This is usually possible the day of entry. Under local anesthesia, thoracoscopy is done generally in the anterior axillary line in the second interspace. The lung is carefully inspected for the rupture point. Usually the emphysematous blebs will lie in the upper lobe. At this time fluid, if present, can be withdrawn for culture. Through the thoracoscope carrier a No. 18 Foley catheter is inserted and the bag inflated with 5 cc. of sterile saline. The carrier is then withdrawn and the catheter pulled snugly against the chest wall. An occlusive dressing is placed about the catheter. The patient is taken to x-ray and the catheter connected to the suction machine. (The general set-up is illustrated by Figure 1).

Under direct fluoroscopic vision the machine is started at a low pressure of 5 cm. of negative intrapleural pressure. If this is sufficient, the lung will expand completely within five minutes, if not, the pressure may be increased to 10 cm. and on up as necessary with 5 cm. steps until the lung is expanded under fluoroscopic vision. Usually, a pressure below 20 cm. will expand the pneumothorax. Five minutes should be allowed for each pressure as the

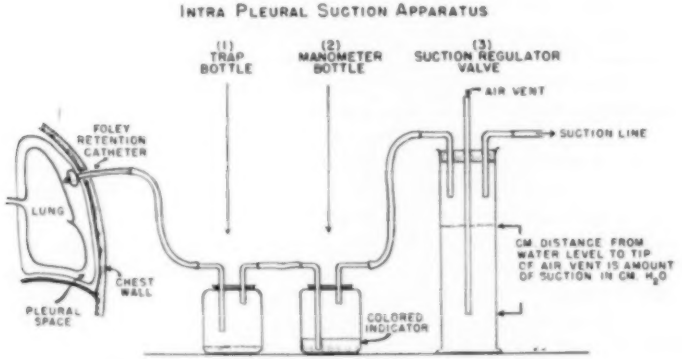

Figure 1: Diagram of intrapleural suction apparatus.

lung may not come out instantaneously, particularly if the collapse has existed for a long period of time. When the lung is expanded, a film is taken, the suction discontinued and the patient returned to the ward where suction is restarted at 25 cm. and this suction is then left on continuously for three days. Since the maximal negative intrapleural pressure thought to be developed in a normal human being is considered to be under 60 cm. of water, we have arbitrarily set 30 cm. of water as the maximum limit to the negative intrapleural pressure that we are willing to use. On the ward the patient is kept in bed and is free to turn from side to side but cannot sit up, the reason for this is that if the catheter is in the second or third interspace and the patient sits up, the pleural air may rise above the catheter point and the pneumothorax may persist in spite of the suction. Parenteral penicillin is given throughout the period of suction as a safeguard. After three days the suction is discontinued, the intercostal catheter clamped, and a portable chest x-ray film is taken. If the lung is properly expanded, the tube is connected to an underwater seal drainage for two days. At this time another film is taken in the x-ray department. If the lung is still expanded, the tube is withdrawn, care being taken not to allow air to enter the chest. The patient is then allowed to walk and after another day is free to go home. He is generally advised to convalesce at home for a week and then is free to resume his employment.

After the suction has been on for a short time, usually no further air will bubble through the machine. This is apparent by looking at the manometer bottle. This means that the lung has been pulled against the chest and the leak sealed. Any reopening of the leak or a second rupture at another site would immediately be apparent by the observation of second air bubbling. Frequently the fluid level in the manometer bottle rises toward the chest side, indicating first, the cessation of the air leak into the pleural space, and second, active resorption of air in the pleural space so that the pressure is actually lower in the pleural space than the regulated machine suction, the difference being the height of the column of fluid in the manometer bottle above its reservoir level.

Clinical Material

Ten patients between 26 and 46 years of age were studied. All entered the San Francisco Veterans Administration Hospital between 1947 and 1949. Five had no previous history of respiratory disease, two had previous pneumothoraces, and two had pneumonia many years previously. One patient had been a severe chronic cougher and had been developing an increasing exercise dyspnea for one year. On entry all 10 had had pain at the onset of their

pneumothorax and eight had a degree of dyspnea as well. Seven of the pneumothoraces were on the right and three on the left side. All patients had over 50 per cent collapse of the involved lung and four of these were over 90 per cent collapsed. Four had fluid on entry on the side of pneumothorax, one of these being a massive hemopneumothorax.

Findings at Thoracoscopy: Four had obvious adhesions; three had large subpleural bullae, two had no discernible disease as seen by thoracoscopy. One thoracoscopy was inadequate.

Illustrative Case Histories

The following case histories are selected to show the use of continuous suction in the treatment of spontaneous pneumothorax and also to show its limitations where other methods must supplement the use of intrapleural suction.

There were six out of the 10 total who had uncomplicated simple pneumothorax and they had quick expansions with uneventful convalescence, all of whom were returned home in less than two weeks and were permitted to work in three weeks. In those cases having serious underlying pulmonary disease or with the addition of such a factor as hemopneumothorax some modifications were necessary. Since this was an untried method the more difficult cases were deliberately sought and included.

Case 5 (O.A.): This patient's course is typical of the six with an easy expansion and uneventful convalescence. Five days prior to admission he noted dull aching chest pain associated with marked dyspnea. He had had no previous episode or respiratory illness. X-ray film (Figure 2a) showed right pneumothorax with collapse considerably over 50 per cent

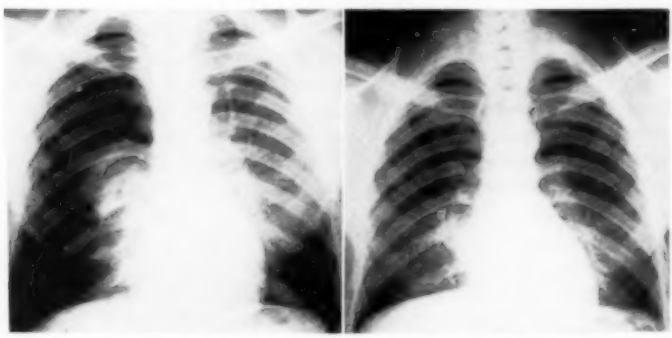

FIGURE 2a FIGURE 2b

Figure 2a: Initial roentgenogram showing right pneumothorax with approximately 75 per cent collapse.
Figure 2b: Roentgenogram six days after initial expansion.

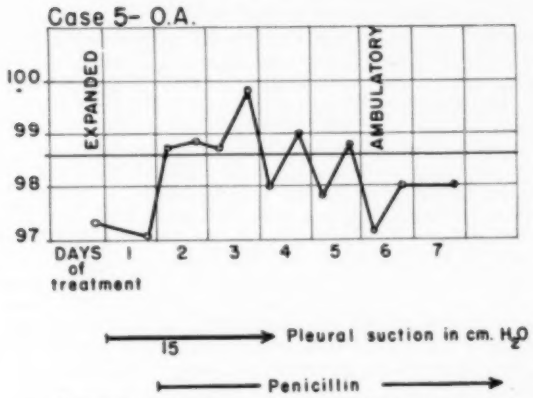

Figure 2c: Patient's course while under treatment.

with a small amount of fluid and slight displacement of the heart and mediastinum toward the left. The left lung appeared normal. On the day of entry thoracoscopy was done and several adhesive bands were noted extending from the anterolateral chest wall to the upper lobe of the right lung. Several small tears were noted at the junction of these fibrous bands with the visceral pleura. Three small rounded areas representing perforations of the visceral pleura were noted at the base of the adhesions in the upper lobe. One of these bubbled slightly when he strained against a closed glottis. A No. 18 Foley catheter was inserted through a thorascope sheath and the lung expanded under direct fluoroscopic control. It was necessary to use 15 cm. of negative pressure of water to expand the lung. The patient was kept at continuous intrathoracic suction of 15 cm. for 72 hours. Then a portable x-ray film showed the lung to be completely expanded. The intrathoracic catheter was placed in an underwater seal for 48 hours, at the end of which time x-ray film showed that the lung remained completely expanded. (Figure 2b shows the x-ray film at that time). The patient's course was singularly uneventful. He suffered no recurrence or dyspnea or chest pain. He was ambulatory on the fifth day following expansion and was discharged from the hospital on the 10th day. He was seen in the follow-up clinic at intervals for 22 months. His lung has remained completely expanded. Figure 2c shows the even temperature course of the patient while under treatment.

Case 1 (T.J.): This 46-year old white male illustrates a collapse after intrapleural suction expansion with a second successful re-expansion. He was the first patient treated and the routine was not yet established. Consequently he was maintained on suction a shorter time than the rest and allowed to be ambulatory at an earlier date. We feel this to have been the cause for the collapse after expansion. He had noted dyspnea six weeks prior to entry and had lost 20 pounds in weight during this time. He had no previous history of respiratory illness. He appeared chronically ill and x-ray films showed an almost complete collapse of the right lower and middle lobe with about 70 per cent collapse of the right upper lobe. There were several apparently cystic areas at the left

apex. After five days of observation he had no further expansion. He was then expanded by continuous intrapleural suction. Subsequent films showed a large bullous cavity in the previously collapsed right apex. He was kept on suction for two days and the lung remained expanded. He was then allowed to be ambulatory but a film the following day showed partial recollapse of the upper and lower lobes. The catheter was reinserted in the second intercostal space and a negative pressure of 20 cm. again instituted, and continued for three days. He was then kept in bed for two more days. An x-ray film at that time showed the lung to be well expanded and it remained so. He developed marked pleuritis and an elevated temperature during the first 10 days after suction. Cultures of the pleural fluid were continuously sterile. The patient steadily improved and was discharged after hospitalization of 32 days. One month after discharge he was feeling well and working. An x-ray film then showed the lung to be completely expanded with a marked regression in the amount of pleuritic change. A follow-up film taken 11 months after the original expansion showed remarkably complete regression of the pleuritic changes.

Case 8 (J.L.): A 27-year old white male required thoracotomy for control of hemorrhage before expansion could be successful. He was perfectly well until 12 hours prior to entry to the hospital. He had no previous relevant cardio-respiratory history. Twelve hours before entry he developed an aching pain in the left chest. He became dyspneic and fainted three times before hospitalization. On examination he appeared pale, moderately sick, quite apprehensive and dyspneic. Chest x-ray film on entry (Figure 3a) showed a fluid level at the left third rib anteriorly with left pneumothorax with more than 50 per cent collapse. The right lung was clear. The mediastinum was displaced slightly to the right.

Thoracoscopy was done on entry and as soon as the trocar was introduced, air and dark unclotted blood gushed from the sheath of the thoracoscope and approximately 1300 cc. of dark unclotted blood was

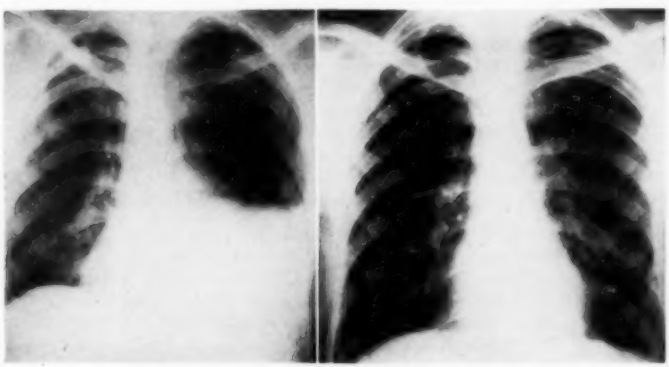

FIGURE 3a FIGURE 3b

Figure 3a: Initial roentgenogram showing left hemopneumothorax with fluid level at third rib anteriorly.

Figure 3b: Roentgenogram taken seven weeks after second expansion.

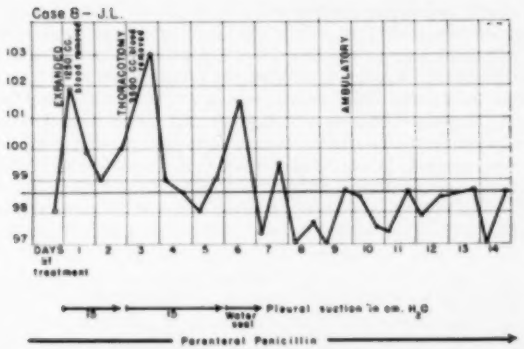

Figure 3c: Patient's course while under treatment.

aspirated from the chest. Subsequent cultures were sterile. Two small punctate areas were noted on the inferior and medial portions of the upper lobe, which exuded air. There were no definite blebs, bullae or frank lacerations. No bleeding points were seen. A No. 18 Foley catheter was inserted into the thoracic cavity. Under fluoroscopic control the lung completely expanded with a negative pressure of 10 cm. of water. He was returned to the ward and kept at this pressure. The day after, his temperature rose to 102 degrees F. and the chest x-ray film showed the lung well expanded. The second day after suction he showed definite evidence of new bleeding within the left thoracic cavity. A chest x-ray film showed complete obliteration of the lung field on that side. He went into frank shock from blood loss. An open exploratory thoracotomy was done through the fifth interspace and approximately 3500 cc. of blood and dark clots were removed from the left thoracic cavity. At this time a small oozing point was noted on the left lateral wall of the thoracic cavity high near the apex. Another small subpleural bleeding point was noted at the apex on the mediastinal side. The chest was closed and anterior and posterior angle tube drains placed into the thoracic cavity. Postoperatively the course was satisfactory and 8 cm. of continuous suction was applied to both of the chest drains. A portable chest x-ray film taken three days after surgery showed the lung to be completely expanded with some evidence of chemical pleuritis. The tubes were connected to an underwater seal. Two days later an x-ray film showed the lung to be in an expanded position. The tubes were removed and he was allowed to be ambulatory. His subsequent course was satisfactory. Figure 3b shows the appearance of the chest x-ray film approximately seven weeks postoperatively. At this time he had returned to work and was comfortable. Again, the striking resolution of the haziness in the chest is noted. Figure 3c shows the summary of the patient's chart. He has been followed for 22 months and remains well.

Case 6 (R.W.): Illustrates a patient whose lung could not be expanded at the maximum possible initial negative pressures and required underwater seal drainage for two days before expansion could be obtained. He was a 28-year old, white male who, while on the ward undergoing treatment for a duodenal ulcer, had sudden severe pain in the right

anterior chest and immediately became dyspneic. He had had spontaneous pneumothorax on the right side in 1944 and a second attack five months before the present episode. The second time he had been confined to bed for 13 days and had required oxygen during the first days of treatment. The initial x-ray film (Figure 4a) showed right pneumothorax with an almost complete collapse of all lobes. At thoracoscopy two definite adhesions were noted near the apex of the upper lobe extending to the anteromedial aspect of the thoracic wall. Several bullae varying from 1 to 4 cm. in diameter were noted on the anterolateral aspect of the upper lobe but with no definite air leak. A hemorrhagic zone was noted between the upper and middle lobes in the anterolateral position. A No.

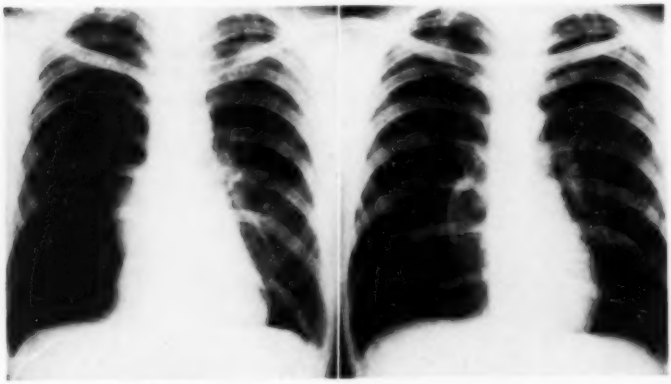

FIGURE 4a FIGURE 4b

Figure 4a: Initial roentgenogram showing complete collapse of the right lung.
Figure 4b: Roentgenogram five weeks after expansion showing complete resolution of the pleuritis.

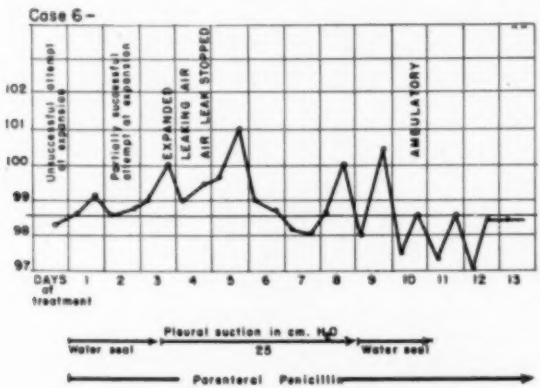

Figure 4c: Patient's course while under treatment.

18 Foley catheter was inserted and under fluoroscopy an attempt made to inflate the lung by negative pressure. This was found to be impossible as the leak from the lung surface was greater than the maximal suction. Suctions to approximately 40 cm. were attempted without expansion of the lung. He was returned to the ward and placed on underwater seal for two days. Repeat x-ray film showed evidence of expansion to perhaps 40 per cent. He was again brought to fluoroscopy and the lung then expanded at minus 25 cm. of water. Subsequently he was kept at this pressure for three days. During this time the suction machine aspirated approximately 600 cc. of amber clear pleural fluid, cultures of which were sterile. After three days, repeat x-ray film showed the lung to be completely expanded. He was then left, as per routine, on underwater seal for two more days. A check x-ray film at this time showed the lung to be fully expanded with evidence of pleural thickening. He experienced some pleural pain from the suciton machine. A subsequent follow-up five weeks after suction (Figure 4b shows a complete resolution of the haziness. Subsequent follow-up for 22 months has shown no evidence of recurrence of the pneumothorax. Figure 4c shows the patient's temperature course in relation to his procedures.

Case 9 (E.L.): Is a therapeutic failure. This patient's lung recollapsed in the second week after expansion. Because of a combination of poor general condition, hematemesis from esophageal varices, and the development of tension pneumothorax, he expired before a second expansion could be made. He was a 43-year old, white male who had noted the onset of dyspnea three weeks prior to entry. Dyspnea became much more severe three days before admission. He had mild pain in the left anterior chest. Past history revealed that he had had chronic morning cough for several years. He had no previous pneumonia or known tuberculosis. He had had no previous spontaneous pneumothoraces. He had been a chronic alcoholic. Physical examination showed a thin, poorly developed male who was quite cyanotic, acutely dyspneic and orthopneic. He was in shock on entry. Examination of his chest showed a lag to the left side with fine rales at the left base. The right lung was clear. Laboratory work showed a hemoglobin of 11 grams and a white count of 11,000 with 59 per cent leukocytes. An entry chest x-ray film showed left pneumothorax with nearly complete collapse. There was a density in the left upper lobe. The right lung showed marked emphysema with basal bullous empyema.

He required oxygen to relieve dyspnea. With bed rest the cyanosis became less but the dyspnea and orthopnea persisted. A repeat x-ray film on the fourth hospital day showed about 50 per cent reexpansion of the left lung. At this time he could barely get along without oxygen. A film on the eighth hospital day showed that the expansion had not increased but there was now a little pleural fluid at the left base. It was felt that this patient could be improved if further expansion of his lung could be attained, it being realized that he was a poor risk. On the ninth hospital day, thoracoscopy was done under local anesthesia. Superficial inspection of the upper lobe showed no bleeding point, or air leak. A No. 18 Foley catheter was introduced into the pleural space. Under fluoroscopic vision the lung was expanded with less than 15 cm. of negative pressure. He was taken back to the ward where the suction was set to 25 cm. of negative pressure, which was maintained for three days. Throughout this time, in spite of the lung being completely ex-

panded, he was still dyspneic and mildly cyanotic, requiring oxygen. Cultures of pleural fluid showed no growth. As a portable x-ray film after three days of suction, showed that the lung was expanded, he was then put on underwater seal for two more days. A chest x-ray film at this time showed that the lung was still expanded. He was then allowed up. A medical consultant stated that he had pulmonary emphysema, chronic alcoholism, no evidence of congestive heart failure and that his dyspnea was due entirely to pulmonary inadequacy. An x-ray film five days after all catheters had been withdrawn from his chest showed the left lung still well expanded and demonstrated yet larger bullae in the right chest. He was then allowed to be ambulatory. He tolerated light activity without dyspnea though he was still slightly cyanotic. On the 19th hospital day he suddenly became comatose. He had hematemesis, some of which had been aspirated. He died before a chest x-ray film could be taken. Necropsy showed that tension pneumothorax had developed on the left. In addition, there were varices and an erosion at the esophageal cardiac junction, which was the source of the bleeding. This case is regarded as a therapeutic failure. Possibly if intrapleural suction had been reinstituted rapidly enough, he might not have died. It is fair to emphasize that his general condition on entry was poor and it had not been possible substantially to improve this condition by any therapeutic measure throughout his hospital course.

Results

Six patients had quick expansion with relatively uneventful convalescences and returned home in less than two weeks and were able to return to work in three weeks. As one patient's lung could not be expanded, he required underwater seal drainage for two days before the lung expanded by the intrapleural suction. His subsequent course was uneventful and follow-up studies to 22 months were satisfactory. One required thoracotomy for control of hemorrhage. Subsequently his lung was expanded by the usual method without complications. Follow-up studies for 22 months showed that his lung was completely expanded. One patient's lung recollapsed after suction was discontinued. His lung was immediately reexpanded. Since that time he has had no recurrence in 26 months. One patient's lung recollapsed during the second week after expansion nine days after the catheters had been removed from his chest. Because of the bleeding from esophageal varices, his poor general condition, and the development of tension pneumothorax, this patient expired before his lung could be reexpanded. All nine patients have been followed for 22 months or longer and have had no recurrences.

SUMMARY

A method of obtaining constant negative intrapleural suction of any desired amount is described. Its application in the treatment of 10 patients with spontaneous pneumothorax is presented. Nine of the 10 patients have had no recurrence of the pneumo-

thorax. One had a recurrence and died because of a combination of the pneumothorax, generalized pulmonary emphysema with bullous emphysema, and hematemesis from esophageal varices before the lung could be reexpanded a second time. It could not be considered a fatality from the method itself. None of the patients developed any permanent deleterious after-effects from the continuous intrapleural suction. Cultures of pleural fluid during the time of continuous intrapleural suction showed no bacterial growth.

While it is true that the majority of lungs collapsed by spontaneous pneumothorax will expand with no treatment except limitation of activity, it is also true that the time of expansion is several weeks and if the collapse is over 50 per cent it may run well over six weeks, representing a substantial economic loss to the patient. The high percentage of recurrences adds weight to our belief that expectant treatment may not be the treatment of choice even in simple spontaneous pneumothorax.

RESUMEN

Se describe un procedimiento para obtener presión negativa constante tan elevada como se desée.

Se presenta la aplicación de este método en el tratamiento de 10 casos de neumotórax espontáneo. Nueve de los 10 enfermos no han tenido recurrencia del neumotórax. Une tuvo recurrencia y murió por causas múltiples además del neumotórax: enfisema pulmonar generalizado, con enfisema buloso, hematemesis por várices esofágicas, antes de que el pulmón pudiera re-expansionarse por segunda vez. Esta no puede considerarse una defunción atribuible al método mismo. Ninguno de los enfermos tuvo consecuencias dañosas de la succión continua. Los cultivos del líquido pleural durante la succión contínua intrapleural, no mostraron crecimiento bacteriano alguno.

Si bien es cierto que la mayoría de los pulmones colapsados por el neumotórax espontáneo se reexpanden sin tratamiento, salvo una limitación de la actividad física, también es cierto que el tiempo que tarden en expanderse es de varias semanas y si el colapso sobrepasa el 50 por ciento puede durar más de seis semanas, lo que representa una pérdida económica considerable para el paciente. La elevada proporción de recurrencias agrega peso a nuestra creencia de que el tratamiento expectante puede no ser el de elección aún en el neumotórax espontáneo simple.

RESUME

Les auteurs décrivent une méthode qui permet d'obtenir une aspiration continue intrapleurale. Ils présentent 10 observations de malades atteints de pneumothorax spontané, à qui ce traite-

ment fut appliqué. Neuf de ces dix malades n'eurent aucune rechute du pneumothorax, l'un d'entre eux fit une rechute et mourut avec un emphysème pulmonaire généralisé, et une hématémèse provenant de varices oesophagiennes. On ne peut considérer ce cas comme entrant dans les statistiques de la méthode ellemême. Aucun des malades n'eut de rechute consécutive à cette aspiration intrapleurale permanente. Il n'y eut aucune infection du liquide pleural au cours de l'aspiration intrapleurale.

Sans doute est-il vrai que dans la majorité des cas, les poumons collabés par un pneumothorax spontané finissent par reprendre leur expansion sans autre traitement qu'un peu de repos. Mais il faut considérer que la période d'expansion dure plusieurs semaines, et que si le collapsus dépasse 50%, cette réexpansion peut s'étendre sur six semaines représentant une perte économique sensible pour le malade. Le grand pourcentage de rechutes s'ajoute à ces constatations pour que les auteurs pensent que le traitement par l'expectative n'est pas le traitement de choix même dans le simple pneumothorax spontané.

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Hemoptysis, Its Significance and Methods of Study*

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This presentation concerning hemoptysis is the result of a study of the incidence of hemoptysis and its causes, in a series of 100 consecutive cases of intrathoracic disease seen by the thoracic surgical service, either as new cases or follow-ups. It also includes a consideration of the diagnostic procedures available and often necessary in order to establish an accurate diagnosis, along with illustrative case reports. By title it excludes all cases of hematemesis, epistaxis, and bleeding originating in the oro-pharyngeal cavity or larynx. It includes all cases of actual or potential primary or secondary pulmonary disease in which hemoptysis would be theoretically possible, except for thoracic trauma and its complications, and except for pulmonary tuberculosis unless in this last instance the diagnosis was established only by operation.

Hemoptysis occurred in 40 per cent of the cases in the series. This along with the distribution of service and private cases, males and females, white and Negro, and the average age are shown in Table I.

In a similar type of study, Adams and Ficarra[1] in 1945, mentioned most of the causes of hemoptysis included in this study, but in discussing the diagnostic procedures indicated, they stated that bronchography was contraindicated, and we disagree with that because of the high incidence of bronchiectasis among pulmonary diseases. Furthermore, they did not mention exploratory thoracotomy as being a diagnostic procedure in selected cases, and it is certain that all would agree today that this is necessary for diagnosis and treatment, again in selected cases. Also Abbott and Hopkins[2] in 1947, made a study of hemoptysis in 1316 cases of pulmonary disease, and found the incidence to be 37 per cent.

Next it might be instructive to review, in an abbreviated form, a classification of primary and secondary pulmonary diseases which might simulate pulmonary tuberculosis and which would have to be considered in the differential diagnosis of hemoptysis, as presented by King:[3]

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A. Infections
1. Tuberculosis
2. Other Bacterial
   Pyogenic, Brucellosis and Tularemia
3. Mycotic
   Actinomycosis
   Blastomycosis
   Coccidioidomycosis and others
4. Rickettsial
5. Virus
6. Parasitic
   Schistosomiasis

B. Inhalations
1. Industrial
   Silicosis and others
2. Other
   Vomitus and Lipiodol
3. Thermal

C. Neoplasms
1. Primary
2. Secondary
3. Generalized

D. Blood Diseases
1. Leukemia
2. Polycythemia
3. Sickle Cell Anemia

E. Generalized Diseases
1. Sarcoidosis
2. Loeffler's Syndrome
3. Rheumatic Fever and others

F. Fibrosis

G. Granulomatosis

H. Bronchiolectasis

I. Circulatory Disturbances
1. Pulmonary Edema
2. Hemosiderosis
3. Emboli and Infarcts

This is a fairly complete list of pulmonary diseases when subdivided still further, but it does not include extrapulmonary diseases such as aortic aneurysm and diseases of the esophagus or other structures in the mediastinum which might give rise to pulmonary disease secondarily, and thus make hemoptysis a

potentiality if not an actuality, and it does not include pulmonary vascular diseases such as arterial aneurysm and arterio-venous fistula.

The types of disease encountered in our series, their incidence and the incidence of hemoptysis in each type are shown in Table II. The diagnosis was proved in nearly all cases except those listed as having hemoptysis of unknown cause.

It will be noted in Table II that bronchiectasis alone or in combination, occurred in 32 per cent of the cases and that carcinoma of the lung occurred in 15 per cent of the cases. Thus, these along with lung abscess accounted for approximately 50 per cent of the group. The high incidence of bronchiectasis would certainly dictate that bronchography is necessary for accurate diagnosis of pulmonary disease in many cases.

Most important is the consideration of the differential diagnostic procedures necessary to establish a diagnosis of intrathoracic disease, whether or not it is associated with hemoptysis. The occurrence of hemoptysis may be considered as incidental and as not having per se any specific diagnostic significance. The diagnostic procedures available are shown in Table III. The use of autopsy has been omitted purposely because the discussion is limited to the methods of diagnosis during life.

Case histories of several patients are presented to illustrate the indications for the use of several of the diagnostic procedures, and to cite in particular cases in which in spite of the performance of many or all of the diagnostic procedures, only one gave the correct diagnosis. The cases to be cited were not all incurred among the 100 reported in the series and several additional cases are described because of the absence of similar important examples in the series.

Case 1: I.M.F., white female, age 58, had been spitting blood for three months when first seen. There was a history of pulmonary tuberculosis with positive sputum at the age of 21. She remained in bed for one year after which she was said to be well. However, she had been having asthma without localization of the wheezing off and on for 10 to 15 years

TABLE I

100 CASES OF INTRATHORACIC DISEASE WITH POTENTIAL HEMOPTYSIS

Hemoptysis	40 per cent	Males	62 per cent
No Hemoptysis	60 per cent	Females	38 per cent
Service	67 per cent	White	55 per cent
Private	33 per cent	Negro	45 per cent

Average Age 46 Years (Extremes 2 to 90 Years)

TABLE II

THE TYPES OF DISEASE AND THE INCIDENCE OF HEMOPTYSIS

	Hemoptysis	No Hemoptysis	Total
Bronchiectasis	10	14	24
Emphysema and Bronchiectasis	1	3	4
Lung Abscess and Bronchiectasis	0	2	2
Asbestosis and Bronchiectasis	1	0	1
Asthma and (?) Bronchiectasis	1	0	1
Carcinoma of Lung	8	7	15
Lung Abscess	4	1	5
Lung Abscess and Empyema	1	0	1
Empyema	1	3	4
Tuberculous Empyema	0	1	1
Pulmonary Tuberculosis	1	4	5
Pneumonitis and Tuberc. Peritonitis	1	0	1
Bronchitis, tuberculous	0	1	1
Bronchitis, acute recurrent	0	1	1
Bronchitis, chronic	1	2	3
Pleurisy with or without Effusion	0	4	4
Spontaneous Pneumothorax	0	3	3
Aortic Aneurysm	0	3	3
Cardiospasm	0	3	3
Pulmonary Fibrosis	0	2	2
Pulmonary Embolus with Abscess	2	0	2
Sarcoid of Lungs	1	0	1
Sarcoid Med. Lymph Nodes	0	1	1
Suture in Bronchial Stump	1	0	1
Blastomycosis of Lung	0	1	1
Stricture Bronchus and Atelectasis	1	0	1
Bronchogenic Cyst Mediastinum	0	1	1
Osteochondroma of Rib	0	1	1
Ca. Esoph. and L. M. Bronchus	0	1	1
Double Sup. Vena Cava	0	1	1
Cause Unknown (Hypertension)	2*	0	2
Cause Unknown (Asthma)	1*	0	1
Cause Unknown (Pleurisy)	1*	0	1
Cause Unknown	1*	0	1
TOTAL	40	60	100

*Cause Unknown Cases equal 12.5 per cent of 40.

TABLE III

DIAGNOSTIC PROCEDURES

1. Routine History and Physical Examination
2. Routine Laboratory Studies
3. Sputum Studies
   - Character and Amount
   - Smears and Cultures
   - Cytological Examinations
4. Gastric Washings
   - Smears and Cultures
5. Fluoroscopy
6. X-ray films in more than one projection
   - Inspiratory and
   - Expiratory films
7. Tuberculin Tests
   - and other Skin Tests
8. Bronchoscopy
9. Bronchography
10. Barium Swallow
11. Pleural Fluid
    - Character and Amount
    - Bacteriological Examinations
    - Cytological Examinations
12. Biopsy of Pleura
13. Biopsy of Lung
14. Biopsy of Lymph Nodes
15. Angiocardiography and Direct Aortic Angiography
16. Artificial Pneumothorax
17. Artificial Pneumoperitoneum
18. Exploratory Thoracotomy

for which no cause had been found. X-ray films of the chest in P-A and lateral views were interpreted as normal except for calcific deposits in the midportion of the left lung field. Bronchoscopy was performed and there was found to be a marked stricture of the left lower lobe bronchus, the lumen being narrowed to 2 mms. in diameter. As a result of this observation it was believed that the left lower lobe must be atelectatic. Therefore she was returned to the x-ray department with a request for fluoroscopy of the chest and for x-ray films to be made with an appropriate technique. Fluoroscopy revealed a marked shift of the mediastinum to the left on inspiration, and additional x-ray films (Figure 1) showed an obvious complete collapse of the left lower lobe. In retrospect, the same shadow could be seen in the P-A film and it could be noted that the left lung field was more aerated than the right. The earliest previous film which could be found was taken two years previously and revealed the same findings. Therefore it is believed that the stricture of the bronchus and resultant atelectasis was possibly present for the duration of the asthma. It is also believed that if the examinations of the chest almost annually since the patient had had active pulmonary tuberculosis, had included fluoroscopy in addition to films, the diagnosis could have been made many years previously. The importance of fluoroscopy in known or suspected intrathoracic disease is apparent.

Case 2: P.C., white female, age 50, was found to have a mass in the inferior posterior mediastinum on routine fluoroscopy and x-ray films

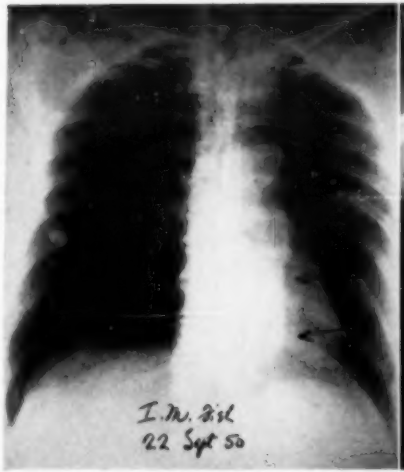

FIGURE 1

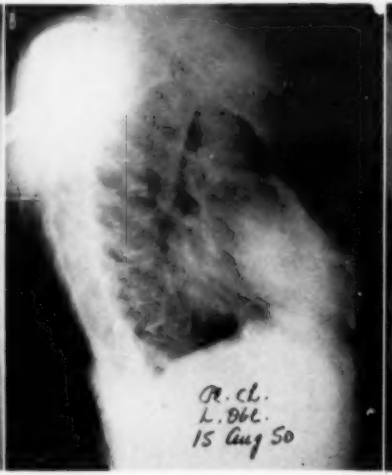

FIGURE 2

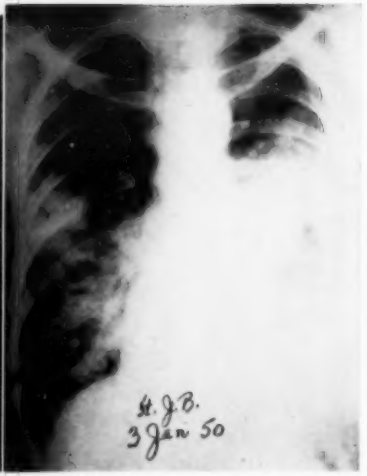

FIGURE 3

Figure 1, Case 1: Atelectasis of the left lower lobe collapsed against the mediastinum as shown in this exposure.—*Figure 2, Case 2:* An oblique view of the chest of a patient showing a large shadow of a mass in the posterior mediastinum which was found to be a bronchogenic cyst.—*Figure 3, Case 3:* X-ray film of the chest revealed extensive bilateral pulmonary disease which was proved by cytological examination of the sputum to be due to carcinoma of the lungs.

of the chest. She had no symptom referable to intrathoracic disease. The film taken in the P-A view appeared to be normal. An oblique view (Figure 2) showed an obvious large mass behind the cardiac shadow, the presence of which is suspected in the P-A view only after observation of the lateral. At operation this proved to be a bronchogenic cyst in the wall of the esophagus. The cyst was removed successfully. This again illustrates the importance of fluoroscopy of the chest in addition to x-ray examination, and the importance of making films in more than one plane.

Case 3: St.J.B., Negro male, age 62, was first seen approximately one year after the onset of an illness characterized by hemoptyses almost daily. X-ray film (Figure 3) revealed extensive bilateral pulmonary disease. A film taken in another hospital at the onset of his illness was essentially the same. At the onset of illness he was treated for tuberculosis including artificial pneumothorax, and also pneumoperitoneum for months even though in spite of adequate search, bacteriological proof of tuberculosis was never obtained. After coming under our observation, six of the first seven sputum specimens submitted for cytological examinations were loaded with malignant cells. Other diagnostic studies, including bronchoscopy and many bacteriological examinations, were non-contributory. The patient died several months later and autopsy revealed extensive multicentric alveolar cell carcinoma in both lungs, with marked exudation of tumor cells into the bronchial tree throughout. It is believed that the performance of cytological examinations of the sputum earlier in the course of his disease would have established the diagnosis many months earlier.

Case 4: L.G., white male, age 37, with a history of severe asthma of 11 years duration, was admitted to the hospital by his physician for study and for consideration of the possibility of some operation for the relief of asthma. The physical examination was not remarkable except for wheezes throughout both lungs. A roentgenogram of the chest (Figure 4) was normal. The study included bronchoscopy which revealed a small non-obstructing ulcer in the left main bronchus. Biopsy of the ulcer revealed carcinoma and he was treated by pneumonectomy with success, in spite of the asthma. It is probable that the presence of the carcinoma of the left main bronchus would not have been detected by any other method of examination prior to the time that it would have become much more advanced.

Because of the high incidence of bronchiectasis among patients with pulmonary disease and among patients with hemoptysis, several examples of the importance of bronchography are cited.

Case 5: S.T., white male, age 50, had x-ray evidence of bilateral apical disease (Figure 5), considered to be tuberculosis, for 17 years. Throughout this time he had numerous episodes of small hemoptyses, and during most of this time literally he remained in bed partly on medical advice and partly because he was scared to get up in view of the fact that activity influenced the incidence of hemoptyses. Bacteriological proof of tuberculosis was never obtained. Among other studies, bronchographic examination (Figure 6) revealed obvious saccular bronchiectasis in both upper lobes, the left greater than the right. Since acid-fast bacilli had never been found in his sputum, it could be considered that the bron-

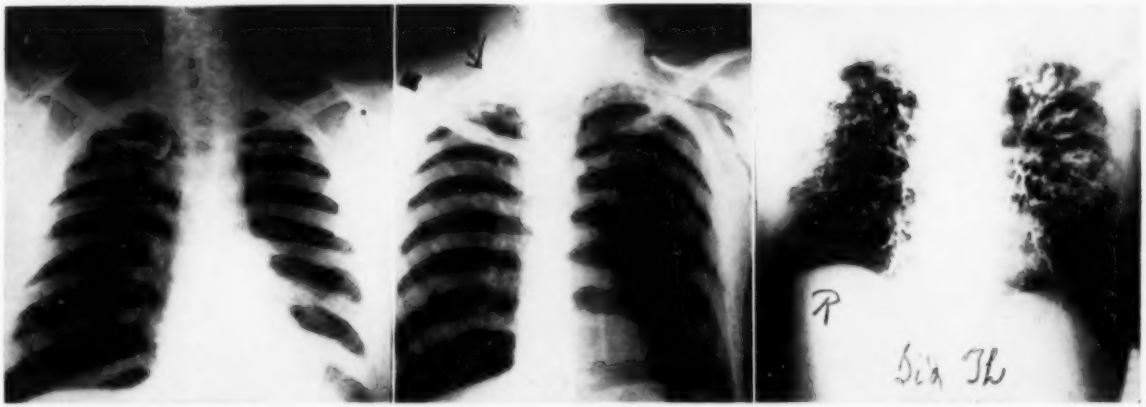

FIGURE 4 FIGURE 5 FIGURE 6

Figure 4, Case 4: X-ray film of the chest of a patient with severe asthma appeared to be normal. However a minute carcinoma of the left bronchus was found on bronchoscopy.—*Figure 5, Case 5:* X-ray film of the chest made 17 years prior to our observation revealed bilateral infiltrative apical disease considered to be tuberculosis.—*Figure 6, Case 5:* Bronchogram of the same patient revealed extensive saccular bronchiectasis in both apices, the left greater than the right.

FIGURE 7 FIGURE 8 FIGURE 9

Figure 7, Case 6: Bronchogram revealing total bronchiectasis on the right. The left lung was normal. — *Figure 8, Case 7:* Bronchogram reveals extensive bronchiectasis in the middle and lower lobes. — *Figure 9, Case 8:* X-ray film of the chest reveals extensive disease primarily in the upper half of both lung fields.

chiectasis was non-tuberculous, and also that the diagnosis could have been made at any time throughout the period of his illness by the use of this diagnostic procedure.

Case 6: C.B., Negro female, age 11, was seen first after a history of chronic pulmonary disease of five years duration. When first seen there was a fairly uniform opacification throughout the right lung field with marked contraction of the right hemithorax. There had been steady progression of the pulmonary disease on the right since the first x-ray film was made at the onset of her illness characterized by cough with purulent sputum and occasional hemoptysis. During the five years she was a patient in a tuberculosis sanatorium and was considered to have pulmonary tuberculosis, although no bacteriological proof of the diagnosis was obtained. In view of the absence of proof of tuberculosis, bronchography was performed and revealed an obvious far-advanced total saccular bronchiectasis of the right lung which was removed successfully (Figure 7). It is apparent that no method of examination other than bronchography would have established the diagnosis with certainty, and that the diagnosis probably could have been established by this procedure at any time subsequent to the onset of her illness.

Case 7: E.W.S., Negro female, age 28, had proved apical tuberculosis on the right of several years duration. In 1947, because of cavitation, she had been treated by a limited thoracoplasty consisting of complete excision of the second, third and fourth ribs. This was followed by closure of the cavity, conversion of the sputum, and complete recovery until shortly before observation in May 1949, at which time she had a recurrence of cough with considerable purulent sputum again positive for acid-fast bacilli. X-ray film inspection of the chest showed a massive cavity in the right upper lobe. The treatment of choice was considered to be upper lobectomy, but since the sputum output seemed to be out of all proportion to that which would be coming from the cavity, and even though the middle and lower lobes appeared to be normal by x-ray, bronchography was performed. Bronchograms (Figure 8) revealed extensive bronchiectasis throughout the middle and lower lobes, thus changing the indicated operation from lobectomy to pneumonectomy. This was performed successfully. It is apparent that the complete diagnoses could not have been established without bronchography and that lobectomy would not have been adequate.

Case 8: W.L.J., white male, age 17, was seen first in April 1950, because of vague pains in the chest and intermittent low-grade fever of five months duration. The remainder of his history was non-contributory and he denied any difficulty in swallowing. Physical examination was normal. An x-ray film of the chest (Figure 9) revealed extensive bilateral pulmonary disease, most marked in the upper half of both lung fields. For the previous three months he had been treated in a tuberculosis sanatorium where an x-ray film on admission showed essentially the same findings. While in the sanatorium bacteriological proof of tuberculosis could not be obtained, therefore he was referred for further study. It was considered that he most likely had sarcoidosis. Various diagnostic procedures, including bronchoscopy, were non-contributory until a barium swallow was obtained for study of the esophagus as part of the routine examination in such cases with obscure pulmonary disease. This (Figure 10) revealed obvious cardiospasm. He still stated that he had no difficulty

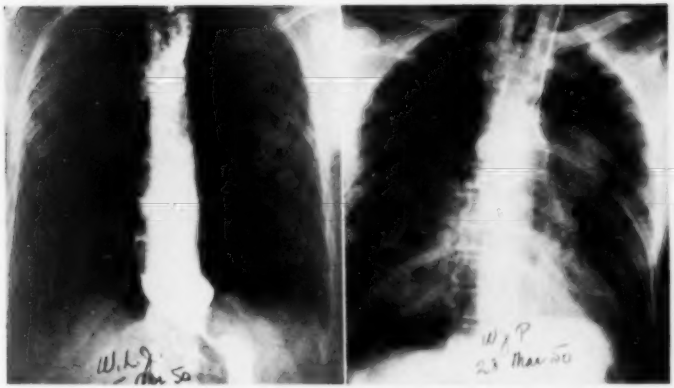

FIGURE 10 FIGURE 11

Figure 10, Case 8: Esophagogram reveals cardiospasm with moderate dilatation of the entire thoracic esophagus.—*Figure 11, Case 9:* Aortic angiogram by direct catheterization reveals no opacification of the shadow.

in swallowing but said he had been awakened frequently at night with attacks of choking and coughing. Therefore it was considered that the pulmonary disease was secondary to aspiration of esophageal contents regurgitated during sleep. Esophagogastrostomy was performed successfully for the relief of the cardiospasm, and he has remained well. It is apparent that the correct diagnosis could not have been established by any other means of examination as simple, and that it could have been established by the use of this method at a much earlier date.

Case 9: W.J.P., white male, age 52, was referred with the diagnosis of aneurysm of the aorta, and possible carcinoma of the lung. He complained of dyspnea, cough and hemoptysis of some months duration. Except for loss of weight and marked emphysema of both lungs, physical examination was not remarkable. X-ray films of the chest revealed a large rounded dense shadow in the left hilum. Fluoroscopy revealed no pulsation, but this did not exclude the possibility of aneurysm. Various diagnostic procedures, including artificial pneumothorax on the left, bronchoscopy, and cytological examinations of the sputum were non-contributory. Therefore, angiocardiography was performed on two occasions using the intravenous injection technique, but for various technical reasons neither examination was satisfactory. Even though from a therapeutic standpoint the diagnosis was immaterial because of the marked degree of pulmonary insufficiency due to the striking generalized bullous emphysema, still it was considered that an accurate diagnosis should be established because oftentimes prognosis is as important as diagnosis. Therefore it was decided to obtain aortic angiograms and this was done by the injection of radio-opaque material through a catheter passed from the superficial temporal artery into the arch of the aorta. The film (Figure 11) revealed a normal arch and descending aorta, and no opacification of the shadow. Therefore aneurysm was excluded in

the differential diagnosis, and carcinoma of the lung was considered to be the correct diagnosis by the process of exclusion.

Case 10: L.W., Negro female, age 33, was admitted to the hospital because of severe pain in the chest of brief duration. Except for slight cyanosis, of which she was unaware, physical examination was entirely

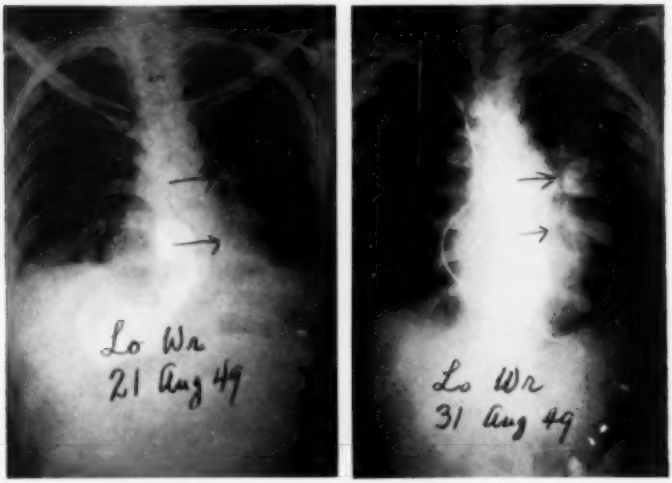

FIGURE 12, Case 10: X-ray film of the chest with and without radio-opaque material injected through a catheter with the tip in the right ventricle revealed obvious opacification of the shadow in the left hilum.

normal. An x-ray film of the chest (Figure 12) revealed bilobular dense shadow of a mass in the left hilum. Other diagnostic studies were noncontributory and because a vascular lesion was suspected, angiocardiography was performed. The x-ray film (Figure 12) revealed an obvious increase in the opacification of the mass, which allowed a correct preoperative clinical diagnosis of pulmonary arteriovenous fistula. This was treated successfully by excision. It is apparent that no method of examination other than exploratory thoracotomy could have established with certainty the correct nature of the lesion.

Case 11: B.O.R., white male, age 46, had symptoms, signs and x-ray evidence (Figure 13) of extensive pulmonary and pleural disease on the left. Various diagnostic procedures, including bronchoscopy, bacteriological and cytological examinations of the sputum, and bacteriological and cytological examinations of the pleural fluid, were noncontributory. Biopsy of the parietal pleura under local anesthesia revealed carcinoma. The tumor was inoperable. The diagnosis could not have been established by so simple a method as operation under local anesthesia without lapse of considerable additional time or even autopsy.

Case 12: A.P., white male, age 40, had a history of recurring cough productive of foul sputum off and on for one year. The examination of the

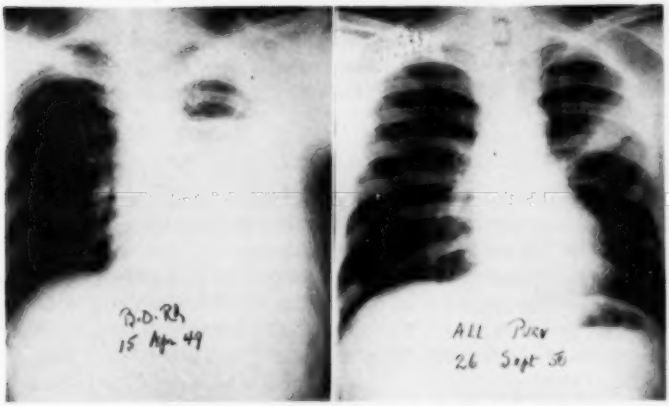

FIGURE 13 FIGURE 14

Figure 13, Case 11: X-ray film of the chest reveals complete opacification of the left lung field except at the apex, due to carcinoma of lung and pleura proven by biopsy of the pleura under local anesthesia.—*Figure 14, Case 12:* The diagnosis of multiple confluent chronic lung abscesses of non-specific etiology in the left upper lobe was established only by thoracotomy and lobectomy.

chest, including x-ray film inspection (Figure 14) indicated extensive infiltration and multiple cavitation in the left upper lobe. All diagnostic procedures were non-contributory and therefore exploratory thoracotomy for diagnosis and treatment was considered necessary, particularly because of the possibility of carcinoma. Left upper lobectomy was performed successfully and multiple chronic lung abscesses of non-specific etiology were found. It is believed that the diagnosis could not have been established with certainty by any other method.

During the five year period, from January 1946 through December 1950, 16 patients have been seen with hemoptysis of undetermined origin. One developed proved tuberculosis two years later. One died eight months later because of hypertension and massive myocardial infarction. At autopsy the lungs revealed only acute pulmonary edema and there was no evidence of neoplasm or other disease to account for the massive hemoptyses experienced eight months prior to death. One case has had further hemoptysis and the cause has not yet been established. The remaining 13 have had no further hemoptysis, although in three other manifestations of pulmonary disease of unknown etiology such as chest pain, cough or asthma have persisted. Four of the 13 had associated systemic hypertension but any possible relation between this and the hemoptysis is not known. It is of interest that only one of the patients has developed proved tuberculosis. In reviewing the records of these patients, however, it is apparent

that many did not have complete study. It is possible that if more of the diagnostic procedures mentioned above had been carried out, it would have been possible to establish diagnoses in many even though the disease may have disappeared or remained asymptomatic since.

SUMMARY

Hemoptysis is of common occurrence during the course of primary or secondary pulmonary disease, having occurred in 40 per cent of the 100 consecutive cases reviewed.

There are many diagnostic procedures, all attended by no risk or remarkably little, which are available for the study of the causes of hemoptysis and the establishment of accurate diagnoses, without which intelligent treatment cannot be instituted.

RESUMEN

La hemoptisis acaece comunmente durante la evolución de enfermedad pulmonar primaria o secundaria, habiendo ocurrido en 40 por ciento de 100 casos consecutivos revisados.

Hay muchos procedimientos de diagnóstico, todos ellos sin riesgo o casi sin él, que pueden aplicarse al estudio de las hemoptisis y para precisar el diagnóstico, sin lo cual un tratamiento inteligente no puede aplicarse.

RESUME

L'hémoptysie apparait fréquemment au cours des affections pulmonaire primitives ou secondaires. Dans 100 cas observés, elle atteint 40% des cas.

Il y a différents procédés de diagnostic, tous caractérisés par l'absence de risque ou le risque minime qu'ils font courir au malade, qui peuvent être utilisés pour l'étude des causes de l'hémoptysie, et pour permettre d'établir un diagnostic convenable sans lequel aucun traitement logique ne peut être institué.

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Pulmonary Fibrosis in Generalized Scleroderma*

Report of a Case and Review of the Literature

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The clinical and roentgenological features of pulmonary fibrosis due to generalized scleroderma were first correlated in 1941 by Murphy, Krainin and Gerson.[1] Since that time there has appeared in the medical literature a number of individual reports of cases with clinically recognized pulmonary involvement. It is our purpose to report another case and to summarize the essential features of such cases which have been reported in the English literature.

Generalized scleroderma is a progressive fibrosing disorder of collagenous tissue, whose signs and symptoms depend upon the organs predominantly involved. It is a clinical and pathological entity whose name belies the fact that originally it was thought to be a disease confined to the skin. It is now recognized that it is a disseminated disease, of unknown etiology, in which the fundamental pathological change is a sclerosing lesion of the connective tissue framework of the skin and other organs. The skin is probably always involved but not necessarily before visceral involvement has progressed to such a state as to give rise to definite signs and symptoms.[2-5] Although the clinical picture is variable the majority of cases begin in one of two ways:[6] (1) gradual onset of Raynaud-like phenomena, usually involving the hands and, sometimes, the feet; (2) an acute or subacute illness which may be quite mild and which is characterized by arthralgia or arthritis, myalgia, often a variable skin eruption and general malaise. Raynaud's phenomena may later appear in cases with this type of onset. Cutaneous changes follow shortly, or, especially in cases with the Raynaud type onset, after an interval of time varying from months to years. There is gradual thickening of the skin of the hands, forearms, face, upper chest, and in some instances the abdomen, feet, and legs. In advanced stages the skin may be shiny, atrophic and bound down to underlying structures. Diffuse generalized pigmentation, or pigmentation localized to the areas of thickening, may occur, and there may be scattered small

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areas of depigmentation in the later stages. The degree of skin involvement is variable and bears no apparent relationship to the degree of visceral involvement. Functional interferences from extensive skin thickening and loss of elasticity include hidebound joints, sclerodactylia, restriction of thoracic movements and difficulty in opening the mouth. Visceral involvement to the extent of producing definite signs and symptoms occurs most commonly in the lungs, heart, esophagus and gastrointestinal tract. Pharyngeal and esophageal dysfunction produce dysphagia and a burning retrosternal or epigastric pain, worse when lying down.[7] Dull epigastric pain, nausea, vomiting and abdominal cramps are related to diffuse fibrous tissue replacement of smooth muscle in the walls of the intestinal tract.[8] The chief symptoms of pulmonary involvement are progressive exertional dyspnea and a slight to moderate productive cough.[2,9] With the development of fibrotic areas in the heart there may occur disturbances in rhythm, cardiac enlargement and signs and symptoms of congestive failure.[3] Although widespread lesions are often found in the kidneys at autopsy, symptoms of renal failure occur only occasionally, and then as a terminal event. It is to be emphasized that in any given case the signs of visceral involvement are usually confined to one or two organs. Symptoms of interference with organ function do not usually occur, especially in pulmonary scleroderma, until the collagenous changes are rather far advanced. Thus, in several cases chest roentgenograms have demonstrated pulmonary fibrosis from several months to several years prior to the development of pulmonary symptoms.

Report of Case

The patient, C. T., a 36 year old coal mine building and maintenance worker, was admitted to the Veterans Administration Hospital, Oteen, North Carolina, on June 12, 1950, because of progressive shortness of breath of two years duration.

Present Illness: The patient, a white World War II veteran, was last in good health in every respect in 1942, the year of his induction into the army. During this year there developed intermittent episodes of coldness, numbness and sweating of the hands and feet. During the following year digital blanching followed by cyanosis and burning pain occurred, often brought on by exposure to cold. During the latter part of 1943 he noticed generalized tanning of the skin, with blotchy areas of deeper brown on the abdomen and back. All of the described changes persisted until his discharge from the service in April 1945. He returned to his pre-war occupation in the coal mine, and later during the same year noted occasional episodes of dull burning epigastric pain and heartburn, usually occurring about an hour after meals. In 1947 there developed gradual progressive weight loss, tiredness, a tendency to gag while eating, and a chronic, slightly productive cough. The weight loss during the 3 years before admission amounted to 40 pounds. In 1948 the patient noticed

exertional dyspnea and occasional fleeting chest pains. There was no hemoptysis. During the two years prior to admission the dyspnea was progressive, and at the time of admission was noticeable even at rest.

Past History: He worked a total of 11 years in the coal mines. There was no history of tuberculosis or contact with this disease. The past medical history was essentially negative before the onset of the present illness. In 1943, about a year after the onset of the Raynaud's phenomena, he was given a six month course of mapharsen and bismuth for seropositive primary syphilis. He received a medical discharge from the army in April 1945, because of multiple fractures sustained in a glider crash.

Physical Examination: The patient was a well developed, undernourished white male, appearing older than the stated age of 36 years. There was slight dyspnea at rest. The face was mask-like and expressionless during the examination. The skin of the forehead was shiny and smooth.

The chest revealed, on inspection, increased antero-posterior diameter, and there was moderate upper dorsal kyphosis. Thoracic movements during respiration were markedly diminished. There was a slight deformity in the right mid-clavicular region due to old fractures of the right first rib and clavicle. Examination of the lungs revealed diminished tactile fremitus and impaired percussion note over the lower one-half of the chest posteriorly, with dullness at the left base. There were many medium and coarse, moist, inspiratory rales heard over the lower half of the chest.

Examination of the heart revealed nothing remarkable. The blood pressure was 110/70. Arterial pulsations were normal in the extremities.

The hands and feet were cold and moist, and the distal halves of the fingers and toes were bluish-purple in color (Figure 1). The tips of the fingers showed small, irregular scars. There were no contractures or immobility of the joints.

The skin of the entire body from the neck to the feet showed increased diffuse brownish discoloration, most marked over the abdomen (Figure 2). Scattered small irregularly shaped areas of depigmentation were seen on the back and forearms. The skin of the forehead, abdomen, hands,

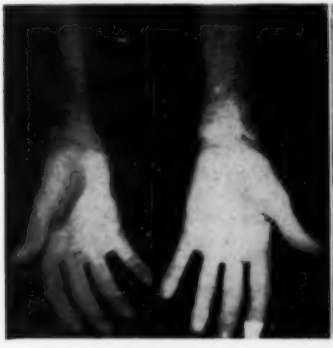

FIGURE 1

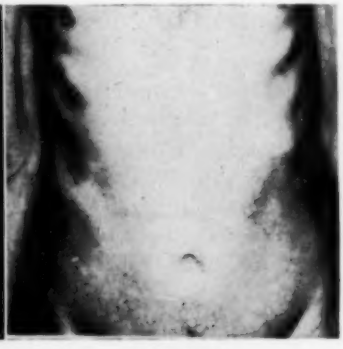

FIGURE 2

Figure 1: Raynaud's phenomenon, involving the hands. Note bluish-purple discoloration of distal portions of fingers.—*Figure 2:* Diffuse pigmentation of the skin, more marked over the lateral abdominal areas.

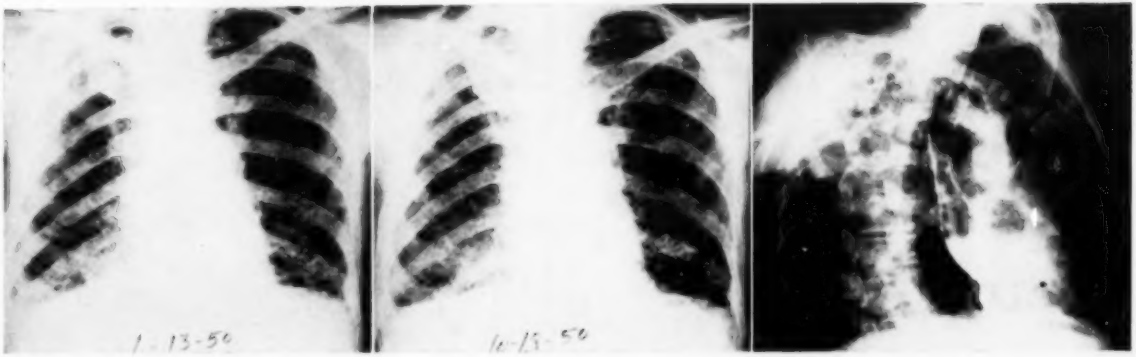

FIGURE 3 FIGURE 4 FIGURE 5

Figure 3: Appearance of chest roentgenogram on admission. Note the diffuse reticular and net-like shadows, lower two-thirds of both lung fields. The increased density of the right upper lung field results from old injury in which there were multiple fractures of clavicle and first rib.—*Figure 4:* Appearance of chest roentgenogram after one month course of para-aminobenzoic acid. There is no essential change.—*Figure 5:* Roentgenogram of esophagus showing narrowing in the lower two inches with dilatation above.

forearms and legs showed moderate diffuse thickening. It was difficult to raise a fold of skin in some of these areas, especially the legs and forehead. It is worthy of note that the patient was unaware that his skin was thicker than normal.

Laboratory Data: Numerous sputum smears, concentrates, cultures and gastric cultures were negative for acid fast bacilli and fungi. A lymph node and a sternal marrow specimen showed normal cytology and were negative for acid fast bacilli on culture. Urinalyses, stool specimens, gastric analysis, serological test for syphilis and basal metabolic rate were negative or within normal limits. A 24 hour urine specimen showed 1090 milligrams of creatinine and 660 milligrams of creatine. The vital capacity was 1600 cc., normal for the patient being 4250.

The following blood studies were within normal limits: fasting sugar, urea nitrogen, alkaline phosphatase, calcium, inorganic phosphorus, sodium, chloride, potassium, uric acid, cholesterol and cholesterol esters, bilirubin, bromsulphalein test and congo red test. The cephalin flocculation test was 3 plus in 48 hours. Serum proteins, on repeated studies showed an increase in the globulin fraction, the globulin varying from 3.4 to 4.8 grams per hundred cc. of blood. The white blood count was persistently higher than normal, ranging from 12,600 to 18,000 on numerous counts. The differential count was essentially normal except for a slight eosinophilia on three occasions.

Bronchoscopic examination was negative. Muscle biopsy (pectoral) showed normal muscle. The following skin tests were negative: coccidioidin, histoplasmin, blastomycin, and first strength tuberculin. Second strength tuberculin test was positive. Special cardiac studies, including electrocardiogram, venous pressure and circulation time, were interpreted as normal.

A skin biopsy from the left forearm showed the dermal collagenous changes and areas of fibrinoid degeneration that are typical of cutaneous scleroderma.

Chest roentgenograms showed a diffuse interstitial fibrosis throughout both lungs, more marked at the bases, with multiple areas of confluence and what appeared to be cyst formation (Figures 3 and 4). Both costophrenic angles were blunted by old pleuro-diaphragmatic adhesions. The cardiac shadow was within normal limits. Planigrams showed multiple varying sized cysts in both lungs, ranging from a few millimeters up to two centimeters in diameter, with the larger cystic areas occurring in the middle zones of the lungs.

Roentgenographic study of the esophagus and gastrointestinal tract showed a smooth narrowing and constriction in the lower two inches of the esophagus with moderate dilatation above (Figure 5). There was moderate retention of barium in the stomach and delay in passage through the small intestine, associated with a slight disturbance in the intestinal mucosal pattern. Roentgenograms of the bones and joints showed no abnormalities except for those resulting from the old injury to the right upper extremity.

Course in the Hospital: A low grade fever, remitting in type, was observed throughout the hospitalization. After a two week course of aureomycin (one-half gram four times daily) the fever diminished, the cough became less bothersome and the amount of sputum diminished. There was an increased sense of well-being, disappearance of the dyspnea at rest and slight gain in weight. It was felt that this improvement was

TABLE I

TWENTY-SEVEN REPORTED CASES OF ROENTGENOGRAPHICALLY VISUALIZED PULMONARY SCLERODERMA

Reported by		Age at Time of Study	Sex	Duration of Disease	Duration of Pulmonary Symptoms	History of Raynaud's Phenomenon	Pulmonary Antedating Cutaneous Symptoms	Esophageal Involvement Demonstrated
Church and	1	49	F	14 years	6 months	+	0	0
Ellis	2	47	F	9 years	1 year	+†	0	+
Kanee	3	46	F	3 years	None	+	0	+
Mathisen and Palmer	4	23	F	6 years	2 years	+	0	0
Weiss, Stead,	5	54	F	25 years	*	+†	0	+
Warren and Bailey	6	56	M	2 years	2 years	0	+	0
Bevans	7	56	M	1 year	1 month	+	0	0
Linenthal	8	45	F	12 years	2 years	+†	0	0
and	9	39	F	13 years	3 years	+†	0	0
Talkov	10	30	F	3 years	6 months	+†	0	0
	11	56	F	23 years	None	+†	0	+
Bourne	12	60	F	25 years	None	+†	0	+

Reported by		Age at Time of Study	Sex	Duration of Disease	Duration of Pulmonary Symptoms	History of Raynaud's Phenomenon	Pulmonary Antedating Cutaneous Symptoms	Esophageal Involvement Demonstrated
	13	48	F	28 years	1 year	+†	**	+
Lloyd	14	45	F	6 years	6 years	+†	+	0
and	15	55	M	3 years	3 years	+	+	0
Tonkin	16	48	F	13 years	5 years	+†	0	0
Wigley, Edmunds and Bradley	17	56	M	3 years	3 years	+	+	0
	18	55	F	13 years	None	+	0	+
Jackman	19	46	F	6 months	None	+†	0	0
Pugh, Kvale and Margules	20	40	M	15 months	1 year	+†	0	+
Murphy, Krainin and Gerson	21	30	F	6 months	6 months	0	***	0
	22	23	M	10 years	10 years	+	***	0
Dostrovsky	23	34	F	2 years	None	0	0	0
	24	36	F	20 years	16 years	0	0	0
Fox	25	47	M	8 years	8 years	0	***	+
Goetz	26	42	F	22 years	4 years	+†	0	+
Spain and Thomas	27	65	M	10 years	10 years	+	+	0

†Indicates that Raynaud's phenomenon was the initial manifestation of the disease.

*Masked by cardiac symptoms.

**Cutaneous changes not described.

***Not definitely stated.

largely due to clearing of secondary bronchial infection. After the diagnosis of generalized scleroderma became clear the patient was given a course of therapy with para-aminobenzoic acid, as described by Zarofonetis.[10] The course consisted of oral administration of 2 grams of the drug every two hours for a total of 12 grams daily. Treatment was continued for 30 days, during which time there was no discernible change in the clinical condition or in the chest roentgenograms. He then received a two-week course of cortisone, during which treatment there was a marked sense of well-being, that persisted after completion of the course, but no measurable objective improvement took place. He was discharged, maximum hospital benefits attained, December 19, 1950.

Discussion

A total of 27 cases of pulmonary fibrosis due to scleroderma have been reviewed, and some of the essential clinical features of these have been tabulated (Table I). These cases represent the reported instances of progressive scleroderma with pulmonary involvement visualized by roentgenography. In the majority of cases the abnormal pulmonary shadows were correctly interpreted during life as sclerodermatous involvement of the lungs. In the few cases thought clinically to be due to other diseases incidentally associated with cutaneous scleroderma, post-mortem examination showed the typical interstitial and vascular collagenous changes of visceral scleroderma.

Nineteen of the 27 cases occurred in females, and the majority of patients were in the fourth and fifth decades of life at the time of the study. Typically the patient's first symptom was the development of peripheral vascular phenomena resembling Raynaud's disease, and this was followed in from several months to several years by a variable amount of diffuse symmetrical thickening of the skin of the extremities, face and occasionally the trunk. Some degree of pigmentation usually occurred. The point at which, in the evolution of the disease, the symptoms of pulmonary fibrosis occurred was extremely variable. In seven cases symptoms of pulmonary scleroderma were present before the development of the skin disease or at a time when cutaneous changes were so slight as to escape attention. Raynaud's phenomena preceded pulmonary symptoms in four of these cases, however, while in the remaining three the pulmonary symptoms occurred as the initial manifestation of the disease. In two of the latter, the time interval between interference with respiratory function and obvious cutaneous scleroderma was over two years.[5,11] Weiss, et al., reported nine cases of cardiac involvement in generalized scleroderma, three of which presented cardiac symptoms occurring up to two years before changes in the skin. These authors noted the lack of correlation between severity of skin changes and peripheral vasomotor symptoms on one hand and severity of cardiac involvement on the

other. This same lack of correlation is seen in pulmonary involvement.

In six of the cases listed in Table I, some time after the development of the skin disease, pulmonary fibrosis was demonstrated, but at the time of the study no pulmonary symptoms had developed. In the remaining 14 cases the picture of scleroderma, usually with Raynaud or acrosclerotic features, became established, and after a variable period of time respiratory symptoms were gradually added to the clinical picture. Characteristically there occurred progressive exertional dyspnea, loss of weight, and usually a slightly productive cough. Hemoptysis was rare, being reported in but one case.[9] Occasionally a low grade fever was observed during hospitalization. Dysphagia and substernal or epigastric pain were complained of in 13 cases (approximately one-half), and in 10 of these roentgen evidence of esophageal involvement was demonstrated.

The roentgenograms of the lungs in the cases reviewed were strikingly similar. The roentgen features of the pulmonary fibrosis of scleroderma have been well described by many of the authors reporting these cases. Early there may be only slight diffuse mottling and interlacing linear shadows, confined to the lower portions of the lungs, and indistinguishable from changes produced by lipoid pneumonia or bronchiectasis. In the more advanced case there is a diffuse and usually symmetrical net-like shadow throughout the lower two-thirds of both lung fields, increasing in density toward the bases. The apices are usually clear. There are also present scattered irregular mottled shadows, usually more prominent in the lower portions. In some cases definite varying sized cysts have been described,[9,12] similar to those in the case we have reported. The cardiac and diaphragmatic contours are often irregular and thickened due to adhesions. It has been stated that in many cases the roentgenologic diagnosis of pulmonary scleroderma can be made without knowledge of the clinical data.[13] Bronchograms have been negative or have shown only minimal bronchiectasis in cases in which bronchography was done.

Of the cases listed in the table, 13 had died at the time of the individual reports of these cases. Of those that died seven were autopsied, and the reports of the findings in these studies form the basis for the following discussion. The essential pathological change found in the lungs was a sclerosing, bulk increasing alteration of the collagen framework. This was noted by Baehr and Pollack to be the essential lesion of scleroderma regardless of its location in the body.[14] The involved lobes were grossly firm and inelastic and some showed reduction in size. Two cases examined by Getzowa showed multiple small cysts, located subpleurally.

Cystic changes have been noted on roentgenograms by other workers.[9,11] Extensive fibrous pleurisy was present, especially involving the lower portions of the lungs. Getzowa's detailed report of the pulmonary findings in two of Dostrovsky's cases describes fully the microscopic features of the disease.[15] Her report also postulates the manner in which the lesions progress and gives an explanation for the cyst formation that occurred. There was described an underlying diffuse alveolar wall fibrosis, with progression, in areas, to massive fibrosis. Marked alveolar wall thickening led to obliteration of capillaries and alveolar spaces. Large coalescing islets of compact fibrous tissue were thus produced, especially in the lower lobes. In other areas hyaline degeneration occurred in the alveolar walls, with disappearance of capillaries. These hyalinized walls became thinned out and ruptured, producing dissolution cysts, and were located near the sub-pleural region. Sub-pleurally there were cystic lesions with fibrous walls and cuboidal or columnar epithelial linings, their formation being referred to as "cystic bronchiolar hyperplasia." Around the bronchi in areas of compact fibrous tissue were adenoma-like lesions, supposedly due to the same process. It is also possible that cystic lesions in this disease are, in part, the result of cystic emphysema. In the case of Church and Ellis in which bronchography was done the iodized oil did not enter the cysts.

Bronchial involvement was described by Spain and Thomas, in their case, the lesions consisting essentially of fibrous replacement of the muscular coat of many of the smaller bronchi, and bronchiolar dilatation. Marked narrowing of the lumina of pulmonary vessels, notably the small arteries and arterioles, has been described by several authors.[8,11,16] Many have noted the widespread occurrence of vascular lesions in scleroderma, and some have attributed the sclerosing lesions of the dispersed connective tissue to the resulting apparent diminution in the blood supply. In most instances there appears to be little correlation between the severity of the vascular changes and the sclerosing lesions in the vicinity of the vessels. In spite of extensive cardiac fibrosis found by Weiss, et al., in their two autopsied cases, the coronary tree was remarkably free of lesions.[3]

The relationship of the pulmonary pathology to the resulting symptomatology has recently been extensively studied by Spain and Thomas.[11] They concluded that respiratory function, e.g., gas exchange over the alveolar interface, was more severely impaired than ventilatory function. Disturbances of the latter, however, due to thoracic skin changes, diaphragmatic involvement and fibrous pleurisy play some part in the production of dyspnea and reduction in vital capacity. The degree of cough and especially

sputum productivity appear to be largely dependent upon bronchitis and respiratory infections to which these patients are particularly prone. It is interesting to note that, with the exception of two cases (numbers 9 and 27 in the table), none of the cases reviewed developed conclusive evidence of right heart failure.

The etiology of scleroderma is unknown. In spite of the fact that it is one of several diseases of unknown etiology which affect the connective tissue framework of the body, the distribution and character of the lesions of generalized scleroderma and the resulting clinical picture are distinctive. Its relationship to other so called collagen diseases, e.g., disseminated lupus erythematosus, dermatomyositis, rheumatic fever, rheumatoid arthritis, serum sickness and polyarteritis nodosa, is still an unsettled question. Certain cases of dermatomyositis have many features that resemble scleroderma.[17] Progressive interstitial fibrosis of the lungs, however, does not occur in dermatomyositis or in any of the other collagen diseases just mentioned.

The disease is chronic and its duration may vary from months to years. After signs and symptoms of pulmonary involvement occur the course is gradually but progressively downhill. The treatment is symptomatic and supportive. Many therapeutic procedures have been tried but none has been shown to significantly alter the progression of the lesions. Among the more recent drugs that have been tried are para-aminobenzoic acid,[10,18] cortisone,[19] and intravenous procaine.[20] In cases with pulmonary involvement early treatment of respiratory infections and preventive measures to minimize the occurrence of such infections are important because of the diminished pulmonary reserve present.

Scleroderma of the lungs, while rare, is being recorded with increasing frequency. When cutaneous manifestations are well established the diagnosis becomes a matter of excluding other conditions which may produce a similar roentgenological picture. In the absence of well defined skin changes the diagnosis is difficult and depends upon an awareness of the condition, some knowledge of the course of the disease and of the sometimes rather typical chest roentgenogram associated with it. When pulmonary fibrosis without obvious reason occurs, scleroderma should be kept in mind and a search made for other evidence of this disease.

SUMMARY

A case of generalized progressive scleroderma, with roentgenologically visualized pulmonary involvement, is reported, and the essential features of such cases that have been reported in the English literature are tabulated and discussed.

Scleroderma of the lungs may clinically antedate the develop-

ment of typical skin changes and present the picture of chronic pulmonary disease. This occurred in approximately one-fourth of the cases reviewed.

Roentgenograms present a picture of net-like interstitial fibrosis of the lower two-thirds of the lungs, sometimes associated with multiple varying sized cysts.

The fundamental pathological changes consist of diffuse alveolar wall sclerosis and alveolar obliteration, cystic changes, in some cases, and vascular narrowing due to involvement of the supporting connective tissue of the vessel walls.

In obscure cases of chronic interstitial fibrosis of the lung, generalized progressive scleroderma should be kept in mind.

The para-aminobenzoic acid used in the treatment of our case was furnished by Wyeth, Incorporated, Philadelphia, Pennsylvania.

We wish to acknowledge the kind assistance and suggestions given by Dr. Ralph E. Moyer, Chief of Tuberculosis Service, Veterans Administration Hospital, Oteen, North Carolina.

RESUMEN

Se relata un caso de escleroderma generalizado progresivo con invasión pulmonar visible a los rayor X y las características esenciales de tales casos referidos en la literatura, son objeto de discusión y de tabulación.

El escleroderma pulmonar puede preceder el desarrollo de cambios típicos en la piel y presentar el aspecto de una enfermedad pulmonar crónica. Esto ocurrió aproximadamente en un cuarto de los casos que se han revisado.

Las radiografías muestran un aspecto parecido a mallas de fibrosis intersticial en los dos tercios inferiores de los pulmones, algunas veces asociadas a quistes de tamaño variable.

Los cambios anatomopatológicos fundamentales consisten en esclerosis difusa de la pared alveolar y obliteración alveolar, formaciones quísticas en algunos casos y estrechamiento vascular debido a la invasión del tejido conectivo de sostén de las paredes de los vasos.

En casos obscuros de fibrosis intersticial de los pulmones, debe tenerse presente la posibilidad de que se trate de un escleroderma generalizado progresivo.

RESUME

Les auteurs rapportent un cas de sclérodermie généralisée progressive, avec des altérations pulmonaires visibles radiologique-

ment. Ils citent et discutent les caractéristiques essentielles de cas semblables publiés dans la littérature anglaise.

Parfois, les altérations peuvent se développer cliniquement avant l'apparition de troubles cutanés; elles réalisent alors un tableau d'affection pulmonaire chronique. Cette éventualité représent approximativement la moitié des observations rapportées. Les radiographies montrent une fibrose interstitielle, aréolaire des deut-tiers inférieurs du poumon; parfois, s'y associent des kystes de dimensions variables.

Les altérations anatomo-pathologiques essentielles consistent en une sclérose diffuse des parois des alvéoles et leur oblitération, la formation de kystes dans certains cas, et le rétrécissement des vaisseaux, du aux modifications du tissu conjonctif des parois vasculaires.

En cas de sclérose interstitielle chronique du poumon de nature indéterminée, il faut toujours avoir présent à l'esprit la possibilité de la sclérodermie progressive généralisée.

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Address on the Occasion of the Second Annual Meeting of the Philippine Chapter of the American College of Chest Physicians May 24, 1951

HERALDO DEL CASTILLO, M.D., F.C.C.P.
President, Philippine Chapter,
American College of Chest Physicians
Manila, Philippine Islands

Today, marks the second year of the existence of the Philippine Chapter, American College of Chest Physicians. The past year was one full of achievements due to the enthusiastic energy of our first President, Dr. Miguel Canizares, whose able leadership is worthy of emulation. He is the first and actual regent of the college for the Philippines; Vice-Chairman, Council on Pan Pacific Affairs; Member, Executive Committee, First International Congress, American College of Chest Physicians, held in Rome, Italy, September, 1950.

At present and perhaps for many more years to come, the problem of tuberculosis will still demand top priority consideration among the many health problems of our country. Notwithstanding an apparent decrease in the mortality rate in tuberculosis in the past few years after liberation (142.73 per 100,000 in 1949 compared to 240 per 100,000 before the war) statistics will show that tuberculosis remains the premier agent in the Philippines of the mighty Grim Reaper. It goes without saying that our government and some of our people realize the sad plight of the tuberculous. All the known methods and available facilities are put into good use in an attempt to stem the tide of this disease.

The educational phase of the anti-tuberculosis program, although not fully organized except in a few urban centers is fast gaining ground and the beneficial effects are being felt by all of us. We can see that the previously uninformed masses are now tuberculosis-minded—a healthy sign of the growing consciousness of our public towards the prevention of this disease. In order to push to the hilt, the educational phase of our work and spread these ideas to the remotest nook and barrio of the archipelago, we would enjoin every physician, every nurse, every teacher and every sanitary inspector to wield their influence in their respective communities so as to teach families how to take care of the sick, how to form and practice correct health habits and teach

them the necessity of a routine yearly x-ray inspection of the chest. The local health officers can and must spearhead this important activity.

The curative phase comprising the surgical and medical management of tuberculosis is in my humble opinion not far behind other countries. Thoracic surgery is availed of to its full advantage and our surgical teams can compare with the best elsewhere. Whatever we lack in facilities is compensated by the resourcefulness, the ardor and the energy of our surgeons. The antibiotics are well known and are widely used by our medical and non-medical practitioners (with emphasis on non-medical), but I would like to join others in raising a finger of warning in the use and abuse of these drugs. There are hundreds of cases we have seen, where streptomycin was used without the benefit of even preliminary radiography and other necessary laboratory examinations. Such a procedure invites danger, as shown by researches along this line from day to day. The latest concept in the use of streptomycin in pulmonary tuberculosis is to give it every second or third day combined with daily oral use of PAS. This procedure seems to lessen the toxicity and possibility of developing the drug resistant strains of M. tuberculosis. We must therefore encourage our colleagues to keep abreast with the modern trends in the therapy of tuberculosis, as well as that of other chest diseases for the sake of our patients.

The Socio-Economic Rehabilitation of the patient, considered an important part of therapy, in the management of the tuberculous is unfortunately lagging very much behind in the scope of our work.

There is a mounting enthusiasm today in the use of BCG vaccine in the Philippines. The authorities concerned with the successful erection of a BCG laboratory in Alabang, considered one of the best three in the world, deserve sincere congratulations and our profound admiration for such a magnificent undertaking. I, for one, cherish the fervent hope that the use of this vaccine may help us control tuberculosis in the Philippines. Nothing could be better than to feel safe from the clutches of this disease after a BCG vaccination. However, Robert Anderson et al., in their paper read before the Annual Meeting, of the National Tuberculosis Association on April 25, 1950, says among other things that:

1) Licensure for the use of BCG would not constitute as an official stamp of approval as to its value as a preventive.

2) Bacteriologists have pointed out that there is little uniformity in the number of viable organisms in the several vaccines now being produced as well as in the different lots of the same vaccine and that there is little knowledge as to how many are viable

at any given time, while the significance of the non-viable present is in the realm of conjecture. Still less is known as to the number of viable organisms required in the injected dose or the question of the minimal or optimal amount necessary to produce the desired conversion.

3) The sensitivity induced by BCG vaccination is not like that which is attributed to natural infection. Lower tuberculin dosages fail to detect the sensitivity in many cases.

4) There is apparent discrepancy about the continued effect of BCG vaccine. It has been said that the protective value of BCG lasts for several years but evidence has shown that the degree of allergy can wane rapidly.

5) Basis for tuberculin test eligibility and interpretation of conversion has wide variations in interpretation.

It is a challenge to our local researchers on BCG to help in the solution of these problems.

The case finding program is going on at a fast rate. We have at present several units making surveys in the different parts of the Islands. But it is our impression that this program should go hand in hand with our ability to provide hospital accommodations for those found harboring this disease.

In connection with this, I would like to take this opportunity of reemphasizing the statement given by the Hon. Secretary of Health during the last Hospital Day, wherein he deplored the paucity of hospital beds in the Philippines. In Tuberculosis work, this condition is more acutely felt. The record shows that in the whole archipelago there are about 1,600 available beds for the tuberculous and most of them are centralized in the City of Manila. Taking our population as 20,000,000 and with the mortality rate of 142.73 per 100,000 as estimated for the year 1949, we have a conservative estimate of around 28,746 Filipinos dying from tuberculosis every year. Considering the ratio of only two beds per death, we ought to have, therefore, at least 56,000 beds for the tuberculous population. We must remember that no less than 300,000 of our people are suffering from active tuberculosis.

The known and accepted method of simple isolation is probably one of the deciding factors for the effective control and prevention of the spread of tubercle bacilli. In the United States and some other smaller countries like Iceland, it is the isolation of cases and existence of better economic conditions that are considered responsible for the success of the control of tuberculosis (140 per 100,000 in 1915 as against 22 per 100,000 in 1950, U. S. Statistics). Iceland, whose inhabitants came originally from the Scandinavian countries, has reduced its mortality rate from 203 per 100,000 in 1929 to 26 in 1949 without the benefit of BCG. Even in Denmark

where the death rate has declined from 174 in 1918 to 30 in 1947, many feel that this success could not be fully attributed to BCG alone as the effects of improved economic conditions and standard methods of prevention cannot be ignored. Not forgetting other phases of tuberculosis control, it is still sufficient beds and better economic conditions for the tuberculous that solved mainly, their problem.

It is not for us on this occasion to discuss ways and means of improving our situation. We know that the time element and availability of funds will be reckoned with. We are all aware that our government is not in a financial condition now to sustain a large scale and an all-out support to put up all the beds we need. We all know that there are more pressing problems before our government at present. But we believe that it is high time for all of us to devote special attention to this phase of our work if we want to save many of our tuberculous and at the same time prevent spreading the disease to their neighbors. If our patients are confined in Sanatoria, all the phases in tuberculosis work as educational, curative, preventive and even rehabilitation, could be done at the same time under proper medical control.

My appeal therefore, is not only directed to my colleagues, for them to redouble their efforts in the fight against this disease, but most of all, to all our people, for them to band together and to give more serious thought to this problem. Let us hope that we may develop that spirit of charity towards our fellowmen, if we want to improve the condition of our sick population and thereby make our nation safe to live in for future generations.

The Philippine Chapter of the American College of Chest Physicians, is barely two years old tonight, but all its members, I am certain, will spare no effort and will buckle down to honest endeavor not only in tackling all the multiple problems associated with chest diseases but in helping our Government accomplish its mission against disease. The individual members of our College will serve as a guiding beacon stabbing the darkness of disease, leading the vanguard in the medical cooperative effort to alleviate suffering, to minimize misery, and to soothe the anguish wrought by disease on a people that is just emerging from the horrors of an unspeakable war.

Report of the Joint Committee on Chest X-Ray

PURPOSE OF JOINT COMMITTEE ON DISEASES OF THE CHEST

In establishing a Joint Committee on Diseases of the Chest, the purpose of the American College of Chest Physicians and the American College of Radiology is to exchange ideas and to propose guiding principles on the problems involved in routine chest x-rays in hospitals (general, mental, etc.), and mass chest x-ray programs. The committee agrees: that each physician should be encouraged to have a chest x-ray on all of his patients; that every patient admitted to a hospital, private or public, should have a routine chest x-ray; and that the follow-up for all suspected lesions seen in chest x-ray surveys should be organized very carefully to assure that the patient comes under medical supervision.

LIMITS OF SURVEY

Routine chest x-ray examinations should be defined as those examinations of the chest which are conducted to screen persons with abnormal changes of the chest from persons with normal chests. The examinations are screening diagnostic procedures and are not to be considered as clinical diagnostic examinations. The screening method is for the purpose of detecting the presence or absence of a lesion only.

The size of the film which one uses for screening purposes is not of primary importance. The committee believes in principle, however, that when microfilms have been used, a 14 x 17 inch film is a necessary second step in the screening procedure and the mechanism whereby such is provided in any community shall be determined by the local medical society or the local hospital staff. Survey chest x-rays either in hospitals or in the general population are approved as a screening device if conducted by agenices which utilize well qualified professional and technical personnel and which make sincere efforts to send the positive individuals to qualified local physicians or clinics for proper follow-up.

INTERPRETATION AND REPORT

Interpretation and reporting of medical findings is a medical matter and should bear the signature or identification of the responsible physician.

METHOD OF REPORTING

Method of reporting of chest survey studies: This is a local matter and is by prearranged agreement between the employer and the employee in industrial surveys; in other surveys is in accord with medical ethics, according to local agreement.

TYPE OF REPORTING

Type of reporting: The Committee discourages the reporting of suspicious cases as tuberculosis. It believes this to be a clinical diagnosis. The x-ray interpreter should designate the cases that require immediate follow-up as "urgent". The small film x-ray interpretation is merely an impression.

It should be emphasized that the 14 x 17 inch film is a diagnostic aid and the results derived therefrom are also impressions and not diagnoses. Even the larger film is but one of several examinations necessary in order to establish correct diagnoses.

PROFESSIONAL COMPENSATION

The professional cost of performing routine chest examinations in hospitals: The Joint Committee believes the radiologist and/or chest physician should be compensated just as any other physicians practicing his profession. The procedure is time consuming and places a definite responsibility on the radiologist or chest physician. The Committee likewise felt that in this matter the basic principle of payment is by arrangement between the physician and the hospital or agency involved. In the reading of follow-up films there should also be an individual limit to the number of films which should be read in any one day by one physician and which he should not exceed. The compensation, of course, would have to take into consideration, whether the physician makes the film in addition to interpreting it.

CLOTHING OF PATIENTS

Whether or not a screening examination can be conducted with the patient fully clothed: Since the number of lesions overlooked because of clothing (2 per cent) is considerably smaller than the normal variations of interpretation (Chamberlin, etc.) have demonstrated to exist in the reading of photofluorographic films, it is concluded that the examination of clothed persons is as effective a procedure as examination of the undressed persons. Since examination of the fully clothed persons is an easier procedure as compared with the examination of the undressed persons, the Committee agreed that screening examination may be conducted with the patient fully clothed.

READER'S QUALIFICATIONS

Qualifications of readers in mass chest surveys: It was believed at the present time there was no practical method which could be used to evaluate the qualifications of a particular reader. Studies in this respect are being made at the present time. It is hoped that within a short period of time satisfactory testing methods will be available. The committee therefore agreed to leave this matter open for further discussion.

PROTECTION

The radiation received by all professional, technical and clerical personnel associated with photofluorographic equipment should be continuously monitored by means of film badges or other devices which have been proved to be satisfactory for determining the radiation exposure of personnel.

When an individual receives more than 100 milliroentgens per week, the medical officer in charge of the unit should immediately determine whether the individual has been careless or whether the protective devices of the equipment are at fault.

If the fault lies with the individual, the individual should be informed of the fact and strongly cautioned regarding the dangers of excessive radiation exposure. Failure to regard such warning should be considered as negligence on the part of the individual.

If the fault lies with the equipment or protective devices, the photofluorographic unit should immediately to taken out of commission until such time that measurements of radiation conditions where technical or clerical personnel are required to work will yield radiation exposures less than 100 milliroentgens per week for case loads of 2500 exposures at 95 kv. and 40 ma. seconds (the average exposure per photofluorographic chest film).

CONTINUATION OF STUDY

It is recommended that the Joint Committee arrangement continue and that the Joint Committee meet annually, or at the call of the co-chairmen. In an effort to have the Joint Committee act continuously and without interruption, interim ideas should be sent to the co-chairmen, and an exchange of opinion shuold continue during the intervals between meetings. Recommendations are solicited from all interested in the affairs of the Joint Committee.

JOINT COMMITTEE ON CHEST X-RAY

American College of Radiology

Leo G. Rigler, Minneapolis, Minnesota ..... Chairman
Sydney J. Hawley, Seattle, Washington
Russell H. Morgan, Baltimore, Maryland
E. P. Pendergrass, Philadelphia, Pennsylvania
Paul C. Swenson, Philadelphia, Pennsylvania

American College of Chest Physicians

Otto L. Bettag, Chicago, Illinois ..... Chairman
Robert J. Anderson, Washington, D. C.
Hollis E. Johnson, Nashville, Tennessee
Edward Kupka, Berkeley, California
James H. Stygall, Indianapolis, Indiana

ANNOUNCEMENT

A Tuberculosis Symposium for General Practitioners will be held in Saranac Lake, New York, July 14-18. This symposium, sponsored by the Saranac Lake Medical Society, will cover all aspects of the modern treatment of pulmonary tuberculosis. The speakers and moderators will include the clinical and research staff of the institutions in the Saranac Lake area as well as private practitioners in the village.

The symposium, which has been approved by the American Academy of General Practice for formal credit for its members, will be held during the mornings only. There will be elective activities during the afternoon. The only charge for this symposium will be a $15.00 registration fee. Physicians desiring to bring their families will find good accommodations and many recreational activities in Saranac Lake and vicinity.

Further information can be obtained by writing the Saranac Lake Medical Society, Box 707, Saranac Lake, New York.

Physicians participating in the Postgraduate Course sponsored by the Council on Postgraduate Medical Education, the New Jersey Chapter of the American College of Chest Physicians and the New Jersey Academy of General Practice, February 20, 27 and March 5, 12, 1952.

II International Congress on Diseases of the Chest

A preliminary program for the II international Congress on Diseases of the Chest sponsored by the Council on International Affairs of the American College of Chest Physicians, to be held in Rio de Janeiro, Brazil, August 24-30, 1952, has been released. This scientific program will be presented on Thursday, Friday and Saturday, August 28, 29 and 30. The scientific program of the XII Congress of the International Union Against Tuberculosis will be presented on August 25, 26 and 27. The inaugural session for both congresses will be held on Sunday, August 24.

The following subjects have been accepted to date for the program of the II International Congress on Diseases of the Chest. Additional papers to be presented at the Congress will be published in future issues of the journal.

1) Andrew L. Banyai, Milwaukee, Wisconsin, U.S.A.:
"Pneumoperitoneum Treatment of Non-tuberculous Diseases."
2) Alvan L. Barach, New York, New York, U.S.A.:
"Physiologic Therapy in Chronic Pulmonary Disease, Including Pulmonary Emphysema."
3) M. Bariety and C. Coury, Paris, France:
"Dysacromegalies of Thoracic Origin."
4) Emil Bogen, Olive View, California, U.S.A.:
"Pleural Adhesions, Their Incidence and Significance."
5) Wilhelm Bolt, Cologne, Germany, M. De Almeida, Ceylon and H. Rink, Cologne, Germany:
"Functional Analysis in Thoracic Surgery."
6) M. M. Brea, A. A. Santas and J. L. Martinez, Buenos Aires, Argentina:
"Echinococcus Cyst of the Lung: Surgical Treatment."
7) John F. Briggs, St. Paul, Minnesota, U.S.A.:
"Precordial Migraine."
8) A. A. Carabelli, Trenton, New Jersey, U.S.A.:
"Bronchopulmonary Suppuration: Therapy with the Endoscopic Application of Oleoginous Penicillin."
9) O. Cabral Motta, Rio de Janeiro, Brazil:
"Malignant Tumors of the Chest."
10) B. Carstensen, L. Noviit and A. Odelberg, Oestersund, Sweden:
"Experience with Subclavian Lymphnode Biopsy in the Diagnosis of Certain Intrathoracic Diseases."
11) J. Maxwell Chamberlain, New York, New York, U.S.A.:
"Carcinoma of the Lung: New Surgical Technique."
12) B. H. Cotton, Pasadena, California, U.S.A. and J. R. F. Penido, Rio de Janeiro, Brazil:
"Surgical Treatment of Carcinoma of the Lung."
13) Manoel de Abreu, Rio de Janeiro, Brazil:
(Title to be announced).
14) L. B. Elwell, Brisbane, Australia:
"Successful Treatment of Respiratory Diseases with Continuous Postural Drainage."
15) Louis L. Friedman, Birmingham, Alabama, U.S.A.:
"Pulmonary Insufficiency Resulting from Anthracosilicosis."
16) Ovidio Garcia Rosell, J. J. Arrendondo, C. A. Lopez, V. Narvaez, S. Neyra, V. Rayes N. and A. Vargas C., Lima, Peru:
"Visceral Topography in Pneumoperitoneum."
17) Benjamin M. Gasul, Chicago, Illinois, U.S.A.:
"One-Thousand Cases of Congenital Malformations of the Heart."
18) Maurice Gilbert, Geneva, Switzerland:
"Transitory Pleuropneumonia with Eosinophilic Adenopathy."
19) Alfred Goldman, Beverly Hills, California, U.S.A.:
"The Surgical Management of Carcinoma of the Lung Discovered in X-ray Surveys."

COLLEGE FELLOWS TOUR LATIN AMERICA

Reading left to right: Irving Kane, New York; DeWitt Daughtry, Miami; Edgar Mayer, New York; Arthur Cracovaner, New York; J. Maxwell Chamberlain, New York; Earl Templeton, Miami; and Robert Wallis, New York.

20) Burgess L. Gordon, Philadelphia, Pennsylvania, U.S.A.:
"The Systemic Effects of Intermittent Positive Pressure (Oxygen) Breathing Treatment."
21) Alvis E. Greer, Houston, Texas, U.S.A.:
"Pulmonary Actinomycosis."
22) Paul H. Holinger, Chicago, Illinois, U.S.A.:
"Congenital Anomalies of the Larynx, Tracheobronchial Tree and the Esophagus."
23) M. Ibrahim, Dacca, East Pakistan:
"Bronchogenic Carcinoma in East Pakistan."
24) Chevalier L. Jackson, Philadelphia, Pennsylvania, U.S.A.:
(Title to be announced).
25) J. Jedlicka, Prague, Czechoslovakia:
"The Respiratory System and Visceral Situs Inversus."
26) R. W. Kissane, R. F. Fidler and J. J. Conn, Columbus, Ohio, U.S.A.:
"Variation in the Incidence of the Thrombo-embolic Phenomena in Acute Coronary Thrombosis."
27) F. Koch, Vienna, Austria:
"Serologic Test for Carcinoma."
28) E. Kux, Innsbruck, Austria:
"Thoracoscopic Vagotomy and Sympathicotomy in Duodenal Ulcer."
29) Edwin R. Levine, Chicago, Illinois, U.S.A.:
"Etiology and Treatment of Bronchospastic Diseases."
30) J. Longtin, B. Carasso and B. G. Begin, Montreal, Canada:
"Electrocardiographic Changes Following Pneumoperitoneum."
31) Lopo de Carvalho, Lisbon, Portugal:
"Angiopneumography in Diagnosis."
32) Louis Mark, Columbus, Ohio, U.S.A.:
"Loeffler's Syndrome: Report of Twenty-Three Cases."
33) Edgar Mayer, New York, New York, U.S.A.:
"Advances in the Use of Drugs in Chronic Lung Disease."
34) H. J. Moersch and J. R. McDonald, Rochester, Minnesota, U.S.A.:
"The Significance of Cell Types in the Study of Bronchogenic Carcinoma."
35) J. Arthur Myers, Minneapolis, Minnesota, U.S.A.:
(Title to be announced).
36) Richard H. Overholt, Boston, Massachusetts, U.S.A.:
"Cure and Palliation for Lung Cancer."
37) J. Winthrop Peabody, Washington, D. C., U.S.A.:
"Acute Interstitial Pulmonary Fibrosis."
38) Jas. H. Stygall, Indianapolis, Indiana, U.S.A.:
"Pulmonary Histoplasmosis."
39) H. E. Tebrock, New York, New York, U.S.A.:
"Newer Concepts in the Management of Chronic Beryllosis with ACTH and Cortisone."
40) Harold G. Trimble, Oakland, California, U.S.A.:
"Pulmonary 'Coin' Lesions."
41) A. Omodei-Zorini, Motta, Pigorini and Montanini, Rome, Italy:
"Bronchial Stenosis."

The subjects to be discussed in the program of the XII Congress of the International Union Against Tuberculosis, August 25-27, are as follows:

"Immunity and Tuberculosis,"
Opening report by Arvid Wallgren, Sweden.

"Treatment and Prognosis in Minimal Pulmonary Tuberculosis,"
Opening report by J. Burns Amberson, U.S.A.

"Organization and Results in Regard to the Tuberculosis Campaign of Mass Surveys,"
Opening report by Fernando Gomez, Uruguay.

Physicians and instructors attending the Fifth Annual Postgraduate Course in Diseases of the Chest, held at the Warwick Hotel, Philadelphia, on March 24-28, 1952.

Philadelphia Postgraduate Course

Another successful Postgraduate Course in Diseases of the Chest was held in Philadelphia March 24 through 28, 1952, under the Chairmanship of Dr. Chevalier L. Jackson of the American College of Chest Physicians. It was necessary to limit the enrollment for this postgraduate course to 85 physicians, since a greater number would have taxed the seating capacity of the lecture hall.

The physicians who attended this course came from 24 states, as well as many other countries. The Armour Laboratories, Chicago, and Smith, Kline and French, Philadelphia, assisted in the social program, and a dinner meeting was held jointly with the Laennec Society on Thursday, March 27. The Sixth Annual Postgraduate Course will be held in Philadelphia, March 23 through 27, 1953.

College Fellows Tour Latin America

A group of Fellows of the American College of Chest Physicians have completed a tour of Cuba, the Dominican Republic, Venezuela and Republic of Panama in behalf of the World Medical Association (Photograph of physicians on page 714).

In Cuba the delegation was sponsored by Dr. Jose A. Bustamante and Dr. Antonio Navarrete, Regent of the College for Cuba. Dr. Marcial Martinez received the delegation in the Dominican Republic. In the Republic of Panama the delegation was received by Dr. Gaspar Arosemena and Dr. Augustin A. Sosa, Governor of the College for Panama. Dr. Rafael Castillo and Dr. Jose Ignacio Baldo, Regent of the College for Venezuela, received the delegation in Venezuela. Meetings and conferences were arranged for the group in each of the countries visited. The complete trip was made by Pan-American World Airways. Several of the doctors were accompanied by their wives.

ANNOUNCEMENT

A course in Broncho-Esophagology will be given at Temple University, September 22 to October 3, 1952. The fee is $250. Further information and application blanks are available through Dr. Chevalier L. Jackson, 1901 Walnut Street, Philadelphia 3, Pennsylvania.

The Laennec Society of Philadelphia will award a prize of $200 for the best paper submitted in any field related to diseases of the chest. This prize is open to undergraduates, interns, residents, or Fellows throughout the United States. The work should be original and not a review of literature or of previous contributions. The society does not reserve the right of publication but requests the prize winning paper be presented at one of its regular scientific meetings.

Five copies of the manuscript should be submitted in the customary form for publication, double space and with wide margins. They should be in the hands of the Secretary of the Society, Dr. Katharine R. Boucot, 311 South Juniper St., Philadelphia 7, Pennsylvania, by October 1, 1952.

College Chapter News

ARIZONA CHAPTER

The Arizona Chapter of the American College of Chest Physicians held a luncheon meeting on Saturday, May 3, 1952, in the Saratoga No. 1 Room of the Westward Ho Hotel, Phoenix. After luncheon at 12:00 noon, during which time there was a panel discussion, the following scientific program was presented:

"Isonicotinic Acid Hydrazine in the Treatment of Tuberculosis,"
Edwin R. Levine, Chicago, Illinois.

"Thoracoplasty with Sub-Scapular Paraffin Pack,"
William M. Lees, Chicago.

"Management of the Severe Asthmatic,"
Edwin R. Levine, Chicago.

PERNAMBUCO CHAPTER OF BRAZIL

The Pernambuco Chapter of Brazil held its second Annual Meeting in Fortaleza, State of Ceara, February 29 and March 1.

The following scientific program was presented:

"Pneumoperitoneum in Treatment of Pulmonary Tuberculosis,"
Herodoto Pinheiro Ramos.

"Cystic Shadows in Acute Pulmonary Infections in Children,"
Arthur Eneas Vieira.

"The Effects of Streptomycin Upon Pulmonary Tuberculosis,"
Angelo Rizzo.

"Pulmonary Resection for Chronic Abscess of the Lung,"
Joaquim S. Cavalcanti.

"Epidemiology of Tuberculosis Workers in Banks in Fortaleza,"
Carlos Alberto Studart Gomes.

"The Decrease of Mortality Rate of Tuberculosis in Recife,"
Aldo Vilas Boas.

"Some Aspects of Cavity Behavior Under Surgical Collapse Therapy,"
Joaquim S. Cavalcanti.

"Social Service in a Tuberculosis Hospital,"
Herodoto Pinheiro Ramos.

College News Notes

Dr. P. Jack Sparer has been appointed Instructor, Department of Psychiatry and Neurology, University of Tennessee College of Medicine, Memphis.

Dr. Claude S. Beck has been appointed Professor of Cardiovascular Surgery at Western Reserve University School of Medicine, Cleveland, Ohio. Dr. John S. Mills, President of the University, states that this professorship is the first in its field in any medical school in the country.

Dr. Leonard A. Scheele was sworn in for his second term as Surgeon General of the Public Health Service on April 3.

Book Reviews

Pioneer Doctor. By Lewis J. Moorman. 251 pages. Price $3.75. University of Oklahoma Press, Norman, Oklahoma. 1951.

When the author of this book was born, physicians had almost no knowledge of the various bacteria responsible for certain diseases. They then had keen powers of observation, the clinical thermometer, the stethoscope and the microscope. The science of bacteriology was just being born. Only one year, the bacillus of leprosy had been discovered. No specific biological test was available to aid in the diagnosis of disease. Little was known about endoscopy and the x-ray had not been discovered. During this author's childhood numerous exciting events occurred, particularly in bacteriology. One bacterium after another was announced as having been proved the specific causes of certain diseases. It was not until this author was in medical school that Roentgen announced the discovery of the x-ray and diphtheria and tetanus antitoxin became available. Following his graduation more bacteria were to be discovered such as Spirochaeta pallida. Immunizing agents were developed for such diseases as typhoid and diphtheria. The abdomen, the chest, including the heart, and the brain yielded up many of their secrets to the surgeon. Specific drugs were produced for many of the bacterial diseases. During the 76 years this author has lived, far more progress was made in diagnosis, treatment and prevention of disease than had been accomplished in the previous recorded history of man.

The author has lived through all of this and has been an active participant contributing much of value to this progressive period. Few physicians are alive today who possess so much information gained largely from actual experience and who have made such fine contributions in so many ways as Dr. Lewis J. Moorman. Therefore, it is particularly fitting and indeed fortunate for people everywhere that he wrote *Pioneer Doctor*. In this authentic delightfully written volume is recorded the experiences of one of America's truly great physicians. His fine character and philosophy of life are revealed throughout.

When Lewis Moorman was a child it was their family physician's "fine character, his high place in the community, his hold upon the hearts of the people, his unselfish devotion to duty, his obvious wisdom and his unchallenged authority" that influenced him to go to medical school. He practiced medicine in the country, in small villages, in Indian territory, in a large city, in sanatoriums and in a fine school of medicine. He became president of the National Tuberculosis Association, the American Trudeau Society, dean of a medical school, editor of his State Medical Association official journal, published excellent articles and books on medical subjects, etc., etc. All of these experiences and many more are woven into this fascinating volume.

Although Dr. Moorman's primary interests have been in the field of diseases of the chest for many years he is well informed on many other phases of medicine. Throughout this volume it is plainly obvious that the American system of medicine has far surpassed any other yet devised. Doctor-family relationship as portrayed in this book has played a far more significant role in American medicine than is generally appreciated. It was just this relationship that led Dr. Moorman himself into the field where he has contributed so much to humanity. It has been that same relationship through the years which has caused many other

persons to follow Dr. Moorman's example.

While this book should be read by every physician and all others engaged in health work in any capacity, it is so written that it can be read with great profit by every person interested in the walfare of humanity.

Help Yourself Get Well. A Guide for Tuberculous Patients and Their Families. By Marjorie McDonald Pyle, M.D. Foreword by H. Corwin Hinshaw, M.D., Pp. 235. Cloth. Price $3.00. Appleton-Century-Crofts, Inc., New York, New York, 1951.

A physician's ability to treat a chronic disease and advise others is tremendously enhanced when that physician has been ill from the disease and has overcome it. No amount of schooling or medical practice can substitute for the knowledge gained while combatting a personal attack of a chronic disease. A physician who has had such an experience delves deeper into the disease, makes keener observations and acquires a larger and better store of information than others. Such a physician comes to know the psychology of the patient and thus discusses procedures and problems so understandingly that confidence is nearly always assured. The fact that the physician is recovering or has recovered from a chronic disease inspires confidence and promptly that all-important ideal, physician-patient-family relationship, is established. This often means the winning of half or more of the patient's battle against the disease.

These are some of the reasons that Dr. Marjorie Pyle was the perfect physician to write *Help Yourself Get Well.* While writing this volume she herself was well on the road to recovery from her third bout with clinical tuberculosis. Another reason Dr. Pyle should write this book is that she has been a close student of tuberculosis in its various aspects for a decade. Scholastically she headed her medical school class, she proceeded with a postgraduate fellowship in internal medicine in one of the world's finest institutions, and she served as assistant medical director in an outstanding sanatorium for the tuberculous. She did a large volume of highly scientific research in experimental tuberculosis and participated in the publication of numerous medical articles on such subjects as chemotherapy in tuberculosis. Thus she possesses superb qualifications as an expert in these fields.

Help Yourself Get Well was written primarily for tuberculous patients and their families. No matter how expert the attending physician, there is much that the patient and the family must do to insure recovery. Dr. Pyle has helped many persons get well from tuberculosis; she knows how essential it is for the patient and the family to cooperate in every detail with the physician. This delightfully written volume contains all the fundamental information that any patient and family needs to do their part in achieving the goal.

This book is capable of helping thousands of persons recover from tuberculosis. In accomplishing this end it must be read and reread—it must be studied. It deserves the highest recommendation of physicians in private practice, clinics, hospitals and sanatoriums. For every case of clinical tuberculosis two copies should be made available, one for the patient, and one for the family.

DISEASES OF THE CHEST

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Volume XXI. January - June. 1952

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SUBJECT INDEX

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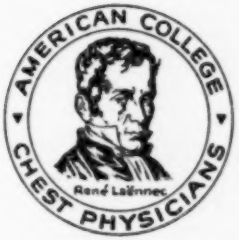

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MURRAY KORNFELD, *Managing Editor*

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MEDICAL SERVICE BUREAU

The facilities of the Medical Service Bureau of the American College of Chest Physicians are available to all who are interested in seeking positions or obtaining applicants in the field of chest diseases. If you wish to advertise in *Diseases of the Chest*, please write to the Medical Service Bureau, American College of Chest Physicians, 112 East Chestnut Street, Chicago 11, Illinois, for rates and further information.

POSITIONS AVAILABLE

Physicians wanted, full time, for new 440 bed tuberculosis division of large general hospital. Associated with two medical schools for teaching purposes; opportunity for research. Complete medical, surgical and pathological facilities. House staff includes straight and rotating internes from general hospital staff. Salary governed by background of training and experience. Please address Box 247A, American College of Chest Physicians, 112 East Chestnut St., Chicago 11, Illinois

Medical Director and Superintendent wanted for 80 bed tuberculosis sanatorium near progressive Southern city. Salary and terms of contract open. Please state qualifications, references and desired salary. Address Box 251A, American College of Chest Physicians, 112 East Chestnut Street, Chicago 11, Illinois.

POSITION WANTED

Thoracic and general surgeon, age 32, has eight years' training, two-and-one-half in thoracic surgery, including tuberculosis and cardiovascular disease, eligible for American Boards of Thoracic Surgery. Passed Part I Surgery. Desires appointment, partnership or institutional appointment with opportunity for private practice. Available at once. Please address Box 266B, American College of Chest Physicians, 112 E. Chestnut St., Chicago 11, Ill.

ELI LILLY AND COMPANY AIDS FLOOD VICTIMS

Eli Lilly and Company, in accordance with its long-established policy, is replacing all Lilly products in pharmacies and hospitals ravaged by the flood in the Missouri and Mississippi River Valleys. Lilly representatives in a dozen states, from Montana to Missouri, have been directed to make the replacement of flood-damaged Lilly pharmaceuticals and biologicals their first order of business.

Along with the replacement of stocks, the Lilly Company maintains

a reserve supply of typhoid vaccine and other biological products which is kept ready for fast shipment during disasters. The shipping personnel of the company stands by twenty-four hours a day.

As the flood waters recede, the replacement of normal stocks will be made as fast as drug stores, hospitals, and wholesale druggists reopen their doors. In the event of a threat of an epidemic, however, needed drugs are shipped directly to the affected area by the fastest possible means of transportation.

NEWS NOTE

The Third Commonwealth and Empire Health and Tuberculosis Conference organized by the National Association for the Prevention of Tuberculosis, will be held in London, July 8-13, 1952. This conference is the third to be held since the war by the National Association for the Prevention of Tuberculosis, which has been active in the campaign for the control of tuberculosis for more than fifty years.

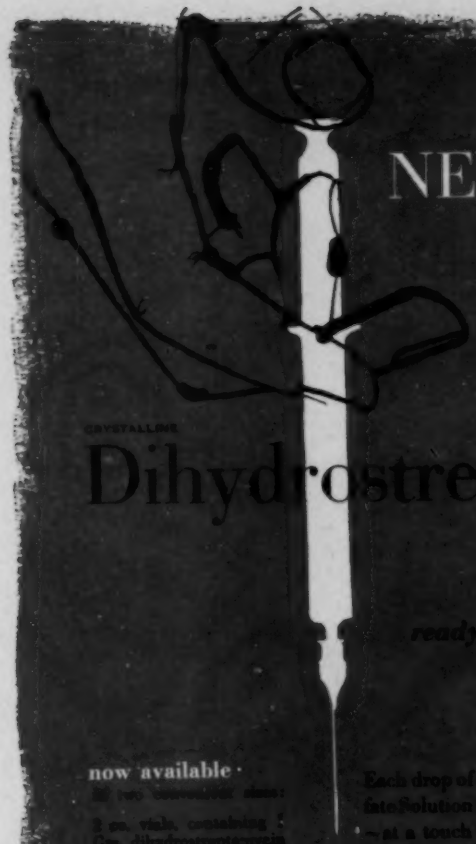
ONTARIO POSTGRADUATE COURSE IN TUBERCULOSIS

The National Sanitarium Association is arranging a four-day postgraduate course in tuberculosis for physicians and surgeons to be held for three days at the Toronto Hospital for Tuberculosis, Weston, with an additional day to include the program for the Annual Meeting of the Ontario Laennec Society to be held at the Royal York Hotel, Toronto. Members of the Faculty of Medicine at the University of Toronto as well as other physicians who are authorities in tuberculosis, will participate in the papers to be delivered as well as in the discussions.

Registration for the Course will be $40, payable to the National Sanitarium Association. That amount will include attendance at all sessions at Weston and in Toronto, transportation between Toronto and Weston, three luncheons and one dinner. This fee should accompany each application.

INTERNATIONAL CONGRESS OF PHYSICAL MEDICINE

The International Congress of Physical Medicine, organized by the British Board of Management of the International Federation of Physical Medicine, will be held in London from July 14 to 19, 1952. Applications for the Provisional Program should be addressed to the Honorary Secretary, International Congress of Physical Medicine (1952) 45, Lincoln's Inn Fields, London, W.C.2.



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